Industria y Comercio

SUPERINTENDENCIA

Delegatura de propiedad Industrial

División de Nuevas Creaciones

PCT

SOLICITUD

PATENTE DE INVENCIÓN

21. **EXPEDIENTE No.** 05-85226

54. **TÍTULO** COMPUESTOS AMINOHETEROARICOS CPMP I INHIBIDORES DE LA PIROTANQUINASOS

51. **CLASIFICACIÓN INTERNACIONAL** AGIK31/4965 AGIP35100

71. **SOLICITANTE** SUGEN, INC.

DOMICILIO 230 EAST GRAND AVENUE, SOUTH SAN FRANCISCO CA 94080-4811, ESTADOS UNIDOS DE AMERICA.

74. **APODERADO** CARLOS R. OLARTE

22. **BOGOTÁ, D. C.,** AGOSTO 25 DE 2005

55

(FORMA P-10)

OLARTERAISBECK

Industria y Comercio
SUPERINTENDENCIA

SUPERINDUSTRIA Y COMERCIO
Radicacion : 05005226 00000000 Folios: 620
Fecha (AMD): 2005-08-26 10:50:23
Tramite : 911 PCT-PATENT 379 FASE NACI 411 PRESENTAC
Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

FORMULARIO ÚNICO DE SOLICITUD DE PATENTE
PCT
ENTRADA EN FASE NACIONAL 26-09-05

(1) SOLICITUD DE:

[X] Patente de Invención. [ ] Patente de Modelo de Utilidad.

[ ] Capítulo I. [X] Capítulo II.

(2) SOLICITANTE (71)

Nombre: SUGEN, INC.
Dirección: 230 East Grand Avenue, South San Francisco, CA 94080-4811 E.U.A.
Nacionalidad o Domicilio: Estadounidense
Lugar de Constitución: San Francisco
Teléfono: _____ Fax: _____
E-mail: _____

IDENTIFICACIÓN
C.C. [ ] NIT [ ]
C.E. [ ] Otro [ ]
Cual _____
Número _____

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IDENTIFICACIÓN
C.C. [X] NIT [ ]
C.E. [ ] Otro [ ]
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Número 79.782.747 Btá
TP 74.295

(4) INVENTOR (ES) (72)

Nombre : VER PAGINA ADJUNTA
Dirección: VER PAGINA ADJUNTA
Nacionalidad o Domicilio: VER PAGINA ADJUNTA Folio 3

(5) PCT (86)

Solicitud Internacional No. PCT/US2004/005495 Fecha Febrero 26, 2004
Publicación Internacional No. WO 2004/076412 Fecha Septiembre 10, 2004

(6) Título (54) COMPUESTOS AMINOHETEROARILOS COMO INHIBIDORES DE LAS PROTEIN QUINASAS

(7) Clasificación Internacional (51) C07D 401/00 A61K 31/4965

(8) Prioridad SI [X] N [ ]

(33) País de Origen	(32) Fecha	(31) Número de Solicitud
US	Febrero 26, 2003	60/449,588
US	Enero 29, 2004	60/540,229

(9) Comprobante de pago No. 60,524 **Fecha** Agosto 12, 2005

(10) **ANEX S**

- [x] Comprobante de pago de la tasa de presentación de la solicitud.
- [ ] Documento que acredita la existencia y representación legal cuando el solicitante sea persona jurídica.
- [x] Poderes, si fuere el caso.
- [ ] Documento de cesión del inventor al solicitante o a su causante.
- [ ] Declaraciones.
- [x] Copia de la solicitud internacional. (Resumen, descripción, reivindicaciones, dibujos).
- [x] Traducción de la solicitud internacional al castellano. (Resumen, descripción, reivindicaciones, dibujos).
- [x] Copia del examen preliminar internacional efectuado por la Autoridad Internacional de Examen Preliminar (IPEA).
- [x] Traducción del examen preliminar internacional efectuado por la IPEA.
- [ ] De ser el caso, copia del contrato de acceso.
- [ ] De ser el caso, documento que acredite la licencia o autorización de uso de conocimientos tradicionales de las comunidades indígenas.
- [ ] De ser el caso, certificado de depósito del material biológico.
- [ ] Arte final 12 x 12.
- [ ] De ser el caso, información sobre otras solicitudes de patente o títulos obtenidos en el extranjero por el mismo titular o su causante, relacionadas parcial o totalmente con la invención de esta solicitud.
- [x] De ser el caso, modificaciones efectuadas a la solicitud internacional.
- [x] Otros. Búsqueda Internacional

(11) **FIGURA CARACTERÍSTICA:**

(12) Solicito la concesión de la patente,

NOMBRE: CARLOS R. OLARTE FIRMA: _____

C.C. 79.782.747 Btá T.P. 74.295

Instrucciones para el diligenciamiento del presente formulario, ver reverso de esta página.

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6

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2

SUPERINDUSTRIA Y COMERCIO
Radicacion : 05005226 00000000
Fecha (AMD): 2005-08-26 10:50:23 Folios: 628
Tramite : 011 PCH-PATENT 379 FASE MACI 411 PRESENTAC
Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

RECIBO OFICIAL DE CAJA : 05 - 60,524
FECHA : AGOSTO 12 DE 2005

***** C O N S I G N A C I O N *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
OLARTE RAISBEGR	CONSIGNACION	BANCO POPULAR	050-00110-6	36579839	11/08/2005	4,518.000.00

***** C O N C E P T O *****

CANT.	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-01 SOLICITUDES	1 TRAMITES DE SOL. DE PATENTE DE IN	443,000.00
		TOTAL : $	443,000.00

SON: CUATROCIENTOS CUARENTA Y TRES MIL PESOS

RESPONSABLE : _____

RECIBO DE CAJA APLICADO AL EXPEDIENTE No._____

Traducción oficial del Inglés por Marlén Neira Castro, resolución 2117 del Ministerio de Justicia de Colombia

APOSTILLA EN PODER DE SUGEN, INC.

APOSTILLA
(Convención de la Haya del 5 de octubre de 1961)

1. País : Estados Unidos de América
   Este documento Público
2. ha sido firmado por Norman Goodman
3. ejerce funciones Secretario de Condado
4. Lleva el sello de condado de Nueva York

CERTIFICADO

5. En Nueva York, Nueva York
6. El 10 de octubre de 2003
7. Por el Secretario de Estado especial suplente, Estado de Nueva York
8. No. NYC- 10088273B
9. Sello del Secretario de Estado de Nueva York
10. Firma de James Bizzarri - Secretario de Estado especial suplente.

CERTIFICACION NOTARIAL

Estado de Nueva York,
Condado de Nueva York N. 348409

Yo, Norman Goodman, Secretario de Condado y de la Corte Suprema de Justicia del Estado de Nueva York, corte de registro con sello legal, certifico por el presente que Jane E. Callahan, cuyo nombre y sello aparecen en el documento, certificado, declaración adjunto, en el momento del reconocimiento ejercía funciones de Notario Público en el Estado de Nueva York, debidamente comisionada, juramentada para actuar como tal, que por ley una comisión o certificado de su carácter oficial, y la firma autógrafa de tal Notario Público se han registrado en mi oficina, que tal Notario estaba autorizado por las leyes de tal Estado a tomar y certificar declaraciones, reconocimientos, y otros instrumentos escritos que deban registrarse; certifico además que estoy familiarizado con la caligrafía del notario público o la comparé con la registrada y considero que la firma puesta en el documento anexo es auténtica. En testimonio de lo anterior, firmo y sello con el sello oficial el día 7 de octubre de 2003. Derechos pagados US $3.

Firma: Norman Goodman-
Secretario de Condado y Corte Suprema de Nueva York- NY.

OCT 2003

MARLEN NEIRA CASTRO
Traductor e Intérprete Ofic
Inglés - Español - Ingl
Resolución No. 2117 del 7 O

CERTIFICACION NOTARIAL

Bilingüe inglés- español, el 4 de Septiembre de 2003 la suscrita notaria certifica que: J. Trevor Lumb, mayor y domiciliado en Estados Unidos firmo el documento anterior, y ejercia funciones de Secretario asistente de Sugen, Inc, domiciliada en San Francisco, California, Estados Unidos.

Que basó las certificaciones 3, 4 y 5 en estos documentos.

Hay sello notarial y firma del notario Jane E. Callahan

Sello Notario Público Estado de Nueva York- No. 01CA4959877- calificada en el condado de Nueva York- su comisión vence el 11- 12- 2005.

PODER

Bilingue ingles- español otorgado por SUGEN, INC. con sede en el número 230 East Grand Avenue, South San Francisco, CA 94080- Estados Unidos, en relación a las patentes, modelos de utilidad y diseños industriales. Firmado por J. Trevor Dumb, Secretario Asistente -

Fecha: 8 septiembre 2003 en Nueva York- NY. Estados Unidos

--

Es traducción del inglés con copia para la traductora. Bogota, octubre 21-2003

MARLEN
Traductor e Intérprete Oficial
Inglés - Español - Inglés
Resolución No. 2117 del 7 Oct 1993

MARLEN NEIRA CASTRO
Traductor e Intérprete Oficial
Inglés - Español - Inglés
Resolución No. 2117 del 7 Oct 1993

28 OCT 2003

D.C. - COLOMBIA

Apostille

(Convention de La Haye du 5 Octobre 1961)

1. Country: **United States of America**

   This public document

2. has been signed by **Norman Goodman**

3. acting in the capacity of **County Clerk**

4. bears the seal/stamp of the county of **New York**

Certified

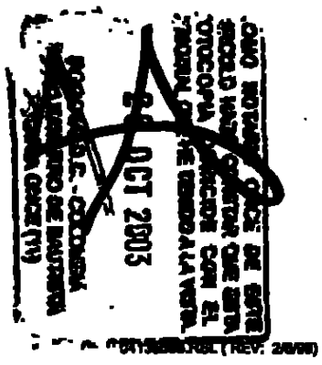
5. At New York, New York 6. the 10th day of October 2003

7. by Special Deputy Secretary of State, State of New York

8. No. NYC-10088273B

9. Seal/Stamp 10. Signature

James Bizzarri
Special Deputy Secretary of State



OLARTERAISBECK

OLARTE RAISBECK & FRIERI, LTDA.
LEGAL & PROFESSIONAL SERVICES

WORLD TRADE CENTER – TORRE C
CALLE 100 NO. 8A-55 PISO 10
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TELEPHONE: +57-1 638-6200
FAX: +57-1 638-6201

www.olarteraisbeck.com

10

Notarial Certification

On this date, September 4, 2003,

The undersigned Notary Public certifies:

1. That J. Trevor Lumb

of legal age and domiciled in USA

signed the foregoing document.

2. That the grantor has executed the foregoing document as Assistant Secretary Of. Susen, Inc.

3. That Susen, Inc., having its principal place of business located in So. San Francisco, Ca., USA, is duly incorporated, is currently in existence, and that the purposes for which the Power of Attorney is granted are within the scope of its corporate purposes.

4. That the grantor has the authority to execute the Power of Attorney and that his/her representation is legal.

5. The foundation for my certifications contained in points 2, 3 and 4 was the exhibition of the following authentic document(s):

Certificación Notarial

En esta fecha,

el Notario Público suscrito certifica:

1. Que

mayor de edad y domiciliado

suscribió el documento que antecede.

2. Que el otorgante ha suscrito el referido documento en su carácter de
de

4. Que
con sede principal ubicada en

está legalmente constituida, que tiene existencia legal vigente y que los propósitos para los cuales se otorga el poder se encuentra dentro de los que comprenden su objeto social.

4. Que el otorgante tiene la representación para suscribir el poder, y que ésta es legítima.

5. El fundamento de mis certificaciones contenidas en los puntos 2, 3 y 4 fue la exhibición de los (del) siguiente(s) documento(s) auténtico(s):

NOTARY PUBLIC (Signature):

JANE E. CALLAHAN
Notary Public, State Of New York
No. 01CA4959877
Qualified In New York County
Commission Expires 12/11/2005

8 OCT 2003

COUNTY CLERK
NEW YORK COUNTY

State of New York,
County of New York, ss.:

Nº 348409

I, NORMAN GOODMAN, County Clerk and Clerk of the Supreme Court of the State of New York, in and for the County of New York, a Court of Record, having by law a seal,
DO HEREBY CERTIFY pursuant to the Executive Law of the State of New York, that

whose name is subscribed to the annexed affidavit, deposition, certificate of acknowledgment or proof, was at the time of taking the same a NOTARY PUBLIC in and for the State of New York duly commissioned, sworn and qualified to act as such; that pursuant to law, a commission or a certificate of his official character, with his autograph signature has been filed in my office; that at the time of taking such proof, acknowledgment or oath, he was duly authorized to take the same; that I am well acquainted with the handwriting of such NOTARY PUBLIC or have compared the signature on the annexed instrument with his autograph signature deposited in my office, and I believe that such signature is genuine.

IN WITNESS WHEREOF, I have hereunto set my hand affixed my official seal this

OCT 07 2003

FEE PAID $3.00

County Clerk and Clerk of the Supreme Court, New York County

OCT 07 2003

CO

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OLARTERAISBECK

OLARTE RAISBECK & FRIERI, LTDA.
LEGAL & PROFESSIONAL SERVICES

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Power of Attorney

The undersigned,

domiciled in

Poder

El suscrito,

SUGEN, INC.

Domiciliado en

230 EAST GRAND AVENUE
SOUTH SAN FRANCISCO, CA 94080
UNITED STATES OF AMERICA

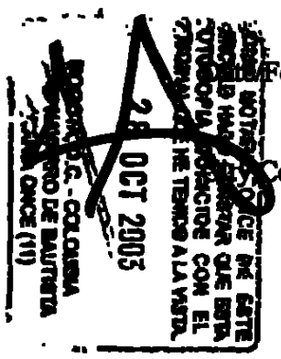
by means of these presents hereby grants to **Carlos R. Olarte and/or Ana María Frieri** full and sufficient Power of Attorney to file, prosecute, obtain, defend and enforce any and all of the company's **Patents, Utility Models and Industrial Designs** in the Republic of Colombia, to which end it empowers them to take all steps necessary before any administrative or judicial authority of any class for the objects stated, to file petitions, appeals, replies and oppositions, pay taxes and annuities, request testimonies, receive documents and securities, abandon applications and collect refunds. Sufficient power is hereby granted to receive notifications on behalf of the Company, to confer powers on those who are to represent the company judicially and extrajudicially, to answer in court in the matter of all claims and demands that may be presented in connection with the objects stated, giving them likewise power to substitute these presents and revoke such substitutions.

por medio del presente otorga a **Carlos R. Olarte y/o Ana María Frieri** poder especial, amplio y suficiente para presentar, tramitar, obtener, defender y hacer respetar todas y cualquiera de **Patentes, Modelos de Utilidad y Diseños Industriales** de la compañía en la República de Colombia, a cuyo efecto los faculta para dar todos los pasos necesarios ante cualquier autoridad administrativa o judicial de cualquier jerarquía para cumplir con lo encomendado, elevar solicitudes, apelaciones, respuestas y oposiciones, pagar impuestos y anualidades, solicitar testimonios, recibir documentos y valores, desistir y percibir. Se concede poder bastante para recibir notificaciones a nombre de la compañía, otorgar poderes a quienes vayan a representar a la compañía judicial y extrajudicialmente, responder en juicio a todas las reclamaciones o demandas que por motivo de lo encomendado se presentaren, dándoles asimismo facultad para sustituir el presente y revocar dichas sustituciones.

Signature/Firma: _____ J. Trevor Lumb, Assistant Secretary
Signature Of Authorized Officer

Date/Fecha: September 8, 2003 (8 September 2003)
Day/Month/Year

City/Country/Ciudad,País: New York, NY USA



(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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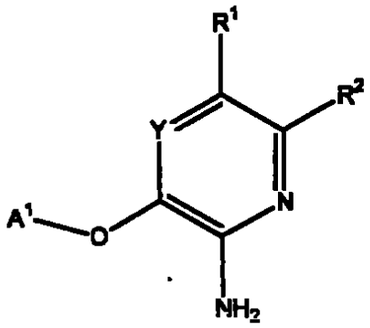
(81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: AMINOHETEROARYL COMPOUNDS AS PROTEIN KINASE INHIBITORS



(1)

(57) Abstract: Aminopyridine and aminopyrazine compounds of formula (I), compositions including these compounds, and methods of their use are provided. Preferred compounds of formula I have activity as protein kinase inhibitors, including as inhibitors of c-MET.

WO 2004/076412 A2

AMINOHETEROARYL COMPOUNDS AS PROTEIN KINASE INHIBITORS

FIELD OF THE INVENTION

The present invention relates generally to novel chemical compounds and methods. More particularly, the invention provides novel aminoheteroaryl compounds, particularly aminopyridines and aminopyrazines, having protein tyrosine kinase activity, and methods of synthesizing and using such compounds.

BACKGROUND

Protein kinases ("PKs") are enzymes that catalyze the phosphorylation of hydroxy groups on tyrosine, serine and threonine residues of proteins. The consequences of this seemingly simple activity are staggering; cell growth, differentiation and proliferation, *i.e.*, virtually all aspects of cell life in one way or another depend on PK activity. Furthermore, abnormal PK activity has been related to a host of disorders, ranging from relatively non-life threatening diseases such as psoriasis to extremely virulent diseases such as glioblastoma (brain cancer).

The PKs can be conveniently broken down into two classes, the protein tyrosine kinases (PTKs) and the serine-threonine kinases (STKs).

One of the prime aspects of PTK activity is their involvement with growth factor receptors. Growth factor receptors are cell-surface proteins. When bound by a growth factor ligand, growth factor receptors are converted to an active form which interacts with proteins on the inner surface of a cell membrane. This leads to phosphorylation on tyrosine residues of the receptor and other proteins and to the formation inside the cell of complexes with a variety of cytoplasmic signaling molecules that, in turn, effect numerous cellular responses such as cell division (proliferation), cell differentiation, cell growth, expression of metabolic effects to the extracellular microenvironment, *etc.* For a more complete discussion, see Schlessinger and Ullrich, *Neuron* 9:303-391 (1992), which is incorporated by reference, including any drawings, as if fully set forth herein.

Growth factor receptors with PTK activity are known as receptor tyrosine kinases ("RTKs"). They comprise a large family of transmembrane receptors with diverse biological activity. At present, at least nineteen (19) distinct subfamilies of RTKs have been identified. An example of these is the subfamily designated the "HER" RTKs, which include EGFR (epithelial growth factor receptor), HER2, HER3 and HER4. These RTKs consist of an extracellular glycosylated ligand binding domain, a transmembrane domain and an intracellular cytoplasmic catalytic domain that can phosphorylate tyrosine residues on proteins.

Another RTK subfamily consists of insulin receptor (IR), insulin-like growth factor I receptor (IGF-1R) and insulin receptor related receptor (IRR). IR and IGF-1R interact with insulin, IGF-I and IGF-II to form a heterotetramer of two entirely extracellular glycosylated α subunits and two β subunits which cross the cell membrane and which contain the tyrosine kinase domain.

A third RTK subfamily is referred to as the platelet derived growth factor receptor ("PDGFR") group, which includes PDGFRα, PDGFRβ, CSFIR, c-kit and c-fms. These receptors consist of glycosylated extracellular domains composed of variable numbers of immunoglobin-like loops and an

intracellular domain wherein the tyrosine kinase domain is interrupted by unrelated amino acid sequences.

Another group which, because of its similarity to the PDGFR subfamily, is sometimes subsumed into the later group is the fetus liver kinase ("flk") receptor subfamily. This group is believed to be made up of kinase insert domain-receptor fetal liver kinase-1 (KDR/FLK-1), flk-1R, flk-4 and fms-like tyrosine kinase 1 (flt-1).

A further member of the tyrosine kinase growth factor receptor family is the fibroblast growth factor ("FGF") receptor subgroup. This group consists of four receptors, FGFR1-4, and seven ligands, FGF1-7. While not yet well defined, it appears that the receptors consist of a glycosylated extracellular domain containing a variable number of immunoglobin-like loops and an intracellular domain in which the tyrosine kinase sequence is interrupted by regions of unrelated amino acid sequences.

Still another member of the tyrosine kinase growth factor receptor family is the vascular endothelial growth factor ("VEGF") receptor subgroup. VEGF is a dimeric glycoprotein similar to PDGF but has different biological functions and target cell specificity *in vivo*. In particular, VEGF is presently thought to play an essential role is vasculogenesis and angiogenesis.

Still another member of the tyrosine kinase growth factor receptor family is MET, often referred to as c-Met, also known as human hepatocyte growth factor receptor tyrosine kinase (hHGFR). c-Met is thought to play a role in primary tumor growth and metastasis.

A more complete listing of the known RTK subfamilies is described in Plowman *et al.*, DN&P, 7(8):334-339 (1994), which is incorporated by *reference*, including any drawings, as if fully set forth herein.

In addition to the RTKs, there also exists a family of entirely intracellular PTKs called "non-receptor tyrosine kinases" or "cellular tyrosine kinases." This latter designation, abbreviated "CTK," will be used herein. CTKs do not contain extracellular and transmembrane domains. At present, over 24 CTKs in 11 subfamilies (Src, Frk, Btk, Csk, Abl, Zap70, Fes, Fps, Fak, Jak and Ack) have been identified. The Src subfamily appear so far to be the largest group of CTKs and includes Src, Yes, Fyn, Lyn, Lck, Blk, Hck, Fgr, AUR1, AUR2 and Yrk. For a more detailed discussion of CTKs, see Bolen, *Oncogene*, 8:2025-2031 (1993), which is incorporated by reference, including any drawings, as if fully set forth herein.

The serine/threonine kinases, STKs, like the CTKs, are predominantly intracellular although there are a few receptor kinases of the STK type. STKs are the most common of the cytosolic kinases; *i.e.*, kinases that perform their function in that part of the cytoplasm other than the cytoplasmic organelles and cytoskeleton. The cytosol is the region within the cell where much of the cell's intermediary metabolic and biosynthetic activity occurs; *e.g.*, it is in the cytosol that proteins are synthesized on ribosomes. The STKs include CDk2, Raf, the ZC family of kinases, the NEK family of kinases, and BUB1.

RTKs, CTKs and STKs have all been implicated in a host of pathogenic conditions including, significantly, cancer. Other pathogenic conditions which have been associated with PTKs include, without limitation, psoriasis, hepatic cirrhosis, diabetes, angiogenesis, restenosis, ocular diseases,

15

rheumatoid arthritis and other inflammatory disorders, immunological disorders such as autoimmune disease, cardiovascular disease such as atherosclerosis and a variety of renal disorders.

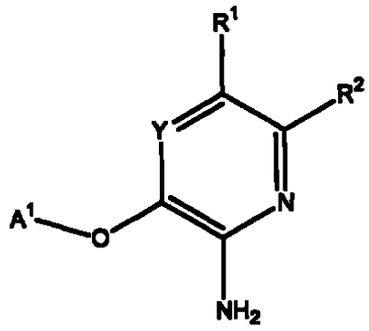
With regard to cancer, two of the major hypotheses advanced to explain the excessive cellular proliferation that drives tumor development relate to functions known to be PK regulated. That is, it has been suggested that malignant cell growth results from a breakdown in the mechanisms that control cell division and/or differentiation. It has been shown that the protein products of a number of proto-oncogenes are involved in the signal transduction pathways that regulate cell growth and differentiation. These protein products of proto-oncogenes include the extracellular growth factors, transmembrane growth factor PTK receptors (RTKs), cytoplasmic PTKs (CTKs) and cytosolic STKs, discussed above.

In view of the apparent link between PK-related cellular activities and wide variety of human disorders, it is no surprise that a great deal of effort is being expended in an attempt to identify ways to modulate PK activity. Some of these have involved biomimetic approaches using large molecules patterned on those involved in the actual cellular processes (*e.g.*, mutant ligands (U.S. Application Serial No. 4,966,849); soluble receptors and antibodies (Application No. WO 94/10202, Kendall and Thomas, *Proc. Nat'l Acad. Sci.*, 90:10705-10709 (1994), Kim, *et al.*, *Nature*, 362:841-844 (1993)); RNA ligands (Jellinek, *et al.*, *Biochemistry*, 33:10450-56); Takano, *et al.*, *Mol. Bio. Cell*, 4:358A (1993); Kinsella, *et al.*, *Exp. Cell Res.*, 199:56-62 (1992); Wright, *et al.*, *J. Cellular Phys.*, 152:448-57) and tyrosine kinase inhibitors (WO 94/03427; WO 92/21660; WO 91/15495; WO 94/14808; U.S. Patent No. 5,330,992; Mariani, *et al.*, *Proc. Am. Assoc. Cancer Res.*, 35:2268 (1994)).

In addition to the above, attempts have been made to identify small molecules which act as PK inhibitors. For example, bis-monocyclic, bicyclic and heterocyclic aryl compounds (PCT WO 92/20642), vinylene-azaindole derivatives (PCT WO 94/14808) and 1-cyclopropyl-4-pyridylquinolones (U.S. Patent No. 5,330,992) have been described as tyrosine kinase inhibitors. Styryl compounds (U.S. Patent No. 5,217,999), styryl-substituted pyridyl compounds (U.S. Patent No. 5,302,606), quinazoline derivatives (EP Application No. 0 566 266 A1), selenaindoles and selenides (PCT WO 94/03427), tricyclic polyhydroxylic compounds (PCT WO 92/21660) and benzylphosphonic acid compounds (PCT WO 91/15495) have all been described as PTK inhibitors useful in the treatment of cancer.

SUMMARY

In one embodiment, the invention provides a compound of formula 1



1

wherein:

Y is N or CR^{12};

R^1 is selected from C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl, 3-12 membered heteroalicyclic, $-O(CR^6R^7)_nR^4$, $-C(O)R^4$, $-C(O)OR^4$, -CN, $-NO_2$, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-C(O)NR^4R^5$, $-NR^4C(O)R^5$, $-C(=NR^6)NR^4R^5$, C_{1-8} alkyl, C_{2-8} alkenyl, and C_{2-8} alkynyl; and each hydrogen in R^1 is optionally substituted by one or more R^3 groups;

R^2 is hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-O(CR^6R^7)_nR^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-C(=NR^6)NR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$, and each hydrogen in R^2 is optionally substituted by one or more R^8 groups;

R^3 is halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-O(CR^6R^7)_nR^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-C(=NR^6)NR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$, each hydrogen in R^3 is optionally substituted by one or more R^8 groups, and R^3 groups on adjacent atoms may combine to form a C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heteroalicyclic group;

each R^4, R^5, R^6 and R^7 is independently hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl; or any two of R^4, R^5, R^6 and R^7 bound to the same nitrogen atom may, together with the nitrogen to which they are bound, be combined to form a 3 to 12 membered heteroalicyclic or 5-12 membered heteroaryl group optionally containing 1 to 3 additional heteroatoms selected from N, O, and S; or any two of R^4, R^5, R^6 and R^7 bound to the same carbon atom may be combined to form a C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic or 5-12 membered heteroaryl group; and each hydrogen in R^4, R^5, R^6 and R^7 is optionally substituted by one or more R^9 groups;

each R^8 is independently halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, -CN, $-O-C_{1-12}$ alkyl, $-O-(CH_2)_nC_{3-12}$ cycloalkyl, $-O-(CH_2)_nC_{6-12}$ aryl, $-O-(CH_2)_n$(3-12 membered heteroalicyclic) or $-O-(CH_2)_n$(5-12 membered heteroaryl); and each hydrogen in R^8 is optionally substituted by one or more R^{11} groups;

A^1 is $-(CR^9R^{10})_n-A^2$ except that:

(i) when Y is N and R^1 is substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl, A^1 is $-(CR^9R^{10})_n-A^2$ and n is not zero; and

(ii) when Y is N and R^2 is H and A^1 is m-chlorobenzyl, R^1 is not unsubstituted piperazine;

each R^9 and R^{10} is independently hydrogen, halogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-NR^4C(O)NR^6R^8$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$; R^9 and R^{10} may combine to form a C_{3-12} cycloalkyl, 3-12 membered heteroalicyclic, C_{6-12} aryl or 5-12 membered heteroaryl ring; and each hydrogen in R^9 and R^{10} is optionally substituted by one or more R^3 groups;

16

A^2 is C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heteroalicyclic, and A^2 is optionally substituted by one or more R^3 groups;

each R^{11} is independently halogen, C_{1-12} alkyl, C_{1-12} alkoxy, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, -O-C_{1-12} alkyl, -O-$(CH_2)_nC_{3-12}$ cycloalkyl, -O-$(CH_2)_nC_{6-12}$ aryl, -O-$(CH_2)_n$(3-12 membered heteroalicyclic), -O-$(CH_2)_n$(5-12 membered heteroaryl) or -CN, and each hydrogen in R^{11} is optionally substituted by one or more groups selected from halogen, -OH, -CN, -C_{1-12} alkyl which may be partially or fully halogenated, -O-C_{1-12} alkyl which may be partially or fully halogenated, -CO, -SO and -SO_2;

R^{12} is hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-O(CR^6R^7)_nR^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-C(=NR^6)NR^4R^5$, $-NR^4C(O)NR^6R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$, and each hydrogen in R^{12} is optionally substituted by one or more R^3 groups;

R^1 and R^2 or R^1 and R^{12} may be combined together to form a C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heteroalicyclic group;

m is 0, 1 or 2;

n is 0, 1, 2, 3 or 4; and

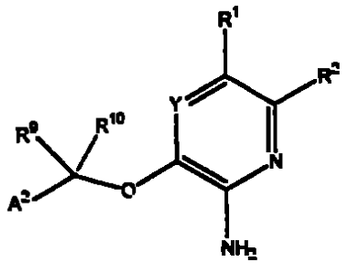
p is 1 or 2;

or a pharmaceutically acceptable salt, solvate or hydrate thereof.

In a particular aspect of this embodiment, Y is N. In a preferred aspect, R^1 is not piperazine. In another preferred aspect, R^1 is not heteroalicyclic.

In another particular aspect of this embodiment, Y is CR^{12}.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment, the compound has formula 1a



1a

wherein A^2 is C_{6-12} aryl or 5-12 membered heteroaryl optionally substituted by one or more R^3 groups.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment, R^1 is selected from C_{6-12} aryl and 5-12 membered heteroaryl, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment not inconsistent with the following definition of R^1, R^1 is selected from C_{3-12} cycloalkyl, 3-12 membered heteroalicyclic, $-O(CR^6R^7)_nR^4$, $-C(O)R^4$, $-C(O)OR^4$, -CN, $-NO_2$, $-S(O)_mR^4$, $-SO_2NR^4R^5$,

$-C(O)NR^4R^5$, $-NR^4C(O)R^5$, $-C(=NR^6)NR^4R^5$, C_{1-8} alkyl, C_{2-8} alkenyl, and C_{2-8} alkynyl; and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment, A^2 is substituted by at least one halogen atom.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment, R^2 is hydrogen, R^9 and R^{10} are independently C_{1-4} alkyl, and A^2 is phenyl substituted by at least one halogen atom.

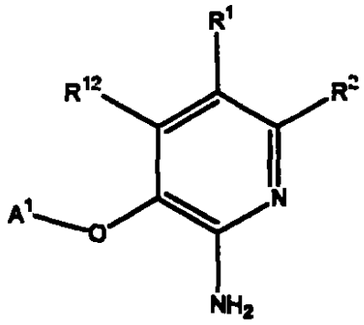
In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment not inconsistent with the following definition of R^1, R^1 is a furan, thiopene, pyrrole, pyrroline, pyrrolidine, dioxolane, oxazole, thiazole, imidazole, imidazoline, imidazolidine, pyrazole, pyrazoline, pyrazolidine, isoxazole, isothiazole, oxadiazole, triazole, thiadiazole, pyran, pyridine, piperidine, dioxane, morpholine, dithiane, thiomorpholine, pyridazine, pyrimidine, pyrazine, piperazine, triazine, trithiane or phenyl group, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment not inconsistent with the following definition of R^1, R^1 is a furan, thiopene, pyrrole, pyrroline, pyrrolidine, dioxolane, oxazole, thiazole, imidazole, imidazoline, imidazolidine, pyrazole, pyrazoline, pyrazolidine, isoxazole, isothiazole, oxadiazole, triazole, thiadiazole, pyran, pyridine, piperidine, dioxane, morpholine, dithiane, thiomorpholine, pyridazine, pyrimidine, pyrazine, triazine, trithiane or phenyl group, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups. In a more particular aspect, R^1 is not heteroalicyclic.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment not inconsistent with the following definition of R^1, R^1 is a fused ring heteroaryl group, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment not inconsistent with the following definition of R^1, R^1 is a $-SO_2NR^4R^5$ group.

In another embodiment, the invention provides a compound of formula 2



2

wherein:

R^1 is selected from C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl, 3-12 membered heteroalicyclic, $-O(CR^8R^7)_nR^4$, $-C(O)R^4$, $-C(O)OR^4$, $-CN$, $-NO_2$, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-C(O)NR^4R^5$,

$-NR^4C(O)R^5$, $-C(=NR^6)NR^4R^5$, C_{1-8} alkyl, C_{2-8} alkenyl, and C_{2-8} alkynyl; and each hydrogen in R^1 is optionally substituted by one or more R^3 groups;

R^2 is hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-O(CR^6R^7)_nR^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-C(=NR^6)NR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$, and each hydrogen in R^2 is optionally substituted by one or more R^8 groups;

R^3 is halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-O(CR^6R^7)_nR^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-C(=NR^6)NR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$, each hydrogen in R^3 is optionally substituted by one or more R^8 groups, and R^3 groups on adjacent atoms may combine to form a C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heterocalicyclic group;

each R^4, R^5, R^6 and R^7 is independently hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl; or any two of R^4, R^5, R^6 and R^7 bound to the same nitrogen atom may, together with the nitrogen to which they are bound, be combined to form a 3 to 12 membered heterocalicyclic or 5-12 membered heteroaryl group optionally containing 1 to 3 additional heteroatoms selected from N, O, and S; or any two of R^4, R^5, R^6 and R^7 bound to the same carbon atom may be combined to form a C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic or 5-12 membered heteroaryl group; and each hydrogen in R^4, R^5, R^6 and R^7 is optionally substituted by one or more R^9 groups;

each R^8 is independently halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, -CN, $-O-C_{1-12}$ alkyl, $-O-(CH_2)_nC_{3-12}$ cycloalkyl, $-O-(CH_2)_nC_{6-12}$ aryl, $-O-(CH_2)_n$(3-12 membered heterocalicyclic) or $-O-(CH_2)_n$(5-12 membered heteroaryl); and each hydrogen in R^8 is optionally substituted by one or more R^{11} groups;

A^1 is $-(CR^9R^{10})_m-A^2$;

each R^9 and R^{10} is independently hydrogen, halogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$; R^9 and R^{10} may combine to form a C_{3-12} cycloalkyl, 3-12 membered heterocalicyclic, C_{6-12} aryl or 5-12 membered heteroaryl ring; and each hydrogen in R^9 and R^{10} is optionally substituted by one or more R^3 groups;

A^2 is C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heterocalicyclic, and A^2 is optionally substituted by one or more R^3 groups;

each R^{11} is independently halogen, C_{1-12} alkyl, C_{1-12} alkoxy, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, $-O-C_{1-12}$ alkyl, $-O-(CH_2)_nC_{3-12}$ cycloalkyl, $-O-(CH_2)_nC_{6-12}$ aryl, $-O-(CH_2)_n$(3-12 membered heterocalicyclic), $-O-(CH_2)_n$(5-12 membered heteroaryl) or -CN, and each hydrogen in R^{11} is optionally substituted by one or more groups selected from halogen,

-OH, -CN, -C_{1-12} alkyl which may be partially or fully halogenated, -O-C_{1-12} alkyl which may be partially or fully halogenated, -CO, -SO and -SO_2;

R^{12} is hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-O(CR^6R^7)_nR^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-C(=NR^6)NR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$, and each hydrogen in R^{12} is optionally substituted by one or more R^3 groups;

R^1 and R^2 or R^1 and R^{12} may be combined together to form a C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heterocalicyclic group;

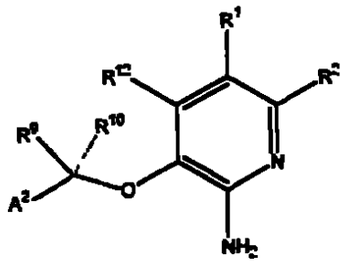
m is 0, 1 or 2;

n is 0, 1, 2, 3 or 4; and

p is 1 or 2;

or a pharmaceutically acceptable salt, solvate or hydrate thereof.

In a particular aspect of this embodiment, the compound has formula 2a



2a

wherein A^2 is C_{6-12} aryl or 5-12 membered heteroaryl optionally substituted by one or more R^3 groups.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment, R^1 is selected from C_{6-12} aryl and 5-12 membered heteroaryl, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment not inconsistent with the following definition of R^1, R^1 is selected from C_{3-12} cycloalkyl, 3-12 membered heterocalicyclic, $-O(CR^6R^7)_nR^4$, $-C(O)R^4$, $-C(O)OR^4$, -CN, $-NO_2$, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-C(O)NR^4R^5$, $-NR^4C(O)R^5$, $-C(=NR^6)NR^4R^5$, C_{1-8} alkyl, C_{2-8} alkenyl, and C_{2-8} alkynyl; and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment, A^2 is substituted by at least one halogen atom.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment, R^2 is hydrogen, R^9 and R^{10} are independently C_{1-4} alkyl, and A^2 is phenyl substituted by at least one halogen atom.

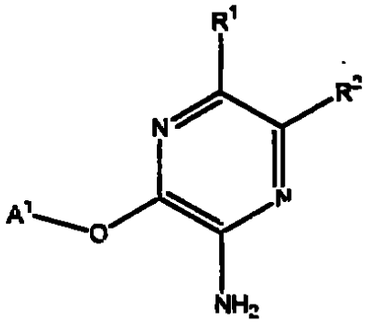
In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment not inconsistent with the following definition of R^1, R^1 is a furan, thiopene, pyrrole, pyrroline, pyrrolidine, dioxolane, oxazole, thiazole, imidazole, imidazoline, imidazolidine, pyrazole, pyrazoline, pyrazolidine, isoxazole, isothiazole, oxadiazole, triazole, thiadiazole, pyran, pyridine,

piperidine, dioxane, morpholine, dithiane, thiomorpholine, pyridazine, pyrimidine, pyrazine, piperazine, triazine, trithiane or phenyl group, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment not inconsistent with the following definition of R^1, R^1 is a fused ring heteroaryl group, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment not inconsistent with the following definition of R^1, R^1 is a $-SO_2NR^4R^5$ group.

In another embodiment, the invention provides a compound of formula 3



3

wherein:

R^1 is selected from C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl, 3-12 membered heterocalicyclic, $-O(CR^6R^7)_nR^4$, $-C(O)R^4$, $-C(O)OR^4$, $-CN$, $-NO_2$, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-C(O)NR^4R^5$, $-NR^4C(O)R^5$, $-C(=NR^6)NR^4R^5$, C_{1-8} alkyl, C_{2-8} alkenyl, and C_{2-8} alkynyl; and each hydrogen in R^1 is optionally substituted by one or more R^2 groups;

R^2 is hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, $-CN$, $-C(O)R^4$, $-OC(O)R^4$, $-O(CR^6R^7)_nR^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-C(=NR^6)NR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$, and each hydrogen in R^2 is optionally substituted by one or more R^8 groups;

R^3 is halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, $-CN$, $-C(O)R^4$, $-OC(O)R^4$, $-O(CR^6R^7)_nR^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-C(=NR^6)NR^4R^5$, $-NR^4C(O)NR^6R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$, each hydrogen in R^3 is optionally substituted by one or more R^8 groups, and R^3 groups on adjacent atoms may combine to form a C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heterocalicyclic group;

each R^4, R^5, R^6 and R^7 is independently hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl; or any two of R^4, R^5, R^6 and R^7 bound to the same nitrogen atom may, together with the nitrogen to which they are bound, be combined to form a 3 to 12 membered heterocalicyclic or 5-12 membered heteroaryl group optionally containing 1 to 3 additional heteroatoms selected from N, O, and S; or any two of R^4, R^5, R^6 and R^7 bound to the same carbon atom may be combined to form a C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12

membered heteroalicyclic or 5-12 membered heteroaryl group; and each hydrogen in R^4, R^5, R^6 and R^7 is optionally substituted by one or more R^8 groups;

each R^8 is independently halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, -CN, -O-C_{1-12} alkyl, -O-$(CH_2)_mC_{3-12}$ cycloalkyl, -O-$(CH_2)_mC_{6-12}$ aryl, -O-$(CH_2)_m$(3-12 membered heteroalicyclic) or -O-$(CH_2)_m$(5-12 membered heteroaryl); and each hydrogen in R^8 is optionally substituted by one or more R^{11} groups;

A^1 is $-(CR^9R^{10})_n-A^2$ except that:

(I) when R^1 is substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl, A^1 is $-(CR^9R^{10})_n-A^2$ and n is not zero; and

(II) when R^2 is H and A^1 is m-chlorobenzyl, R^1 is not unsubstituted piperazine;

each R^9 and R^{10} is independently hydrogen, halogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^6$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_mR^5$ or $-C(O)NR^4R^5$; R^9 and R^{10} may combine to form a C_{3-12} cycloalkyl, 3-12 membered heteroalicyclic, C_{6-12} aryl or 5-12 membered heteroaryl ring; and each hydrogen in R^9 and R^{10} is optionally substituted by one or more R^3 groups;

A^2 is C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heteroalicyclic, and A^2 is optionally substituted by one or more R^3 groups;

each R^{11} is independently halogen, C_{1-12} alkyl, C_{1-12} alkoxy, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, -O-C_{1-12} alkyl, -O-$(CH_2)_mC_{3-12}$ cycloalkyl, -O-$(CH_2)_mC_{6-12}$ aryl, -O-$(CH_2)_m$(3-12 membered heteroalicyclic), -O-$(CH_2)_m$(5-12 membered heteroaryl) or -CN, and each hydrogen in R^{11} is optionally substituted by one or more groups selected from halogen, -OH, -CN, -C_{1-12} alkyl which may be partially or fully halogenated, -O-C_{1-12} alkyl which may be partially or fully halogenated, -CO, -SO and $-SO_2$;

R^1 and R^2 may be combined together to form a C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heteroalicyclic group;

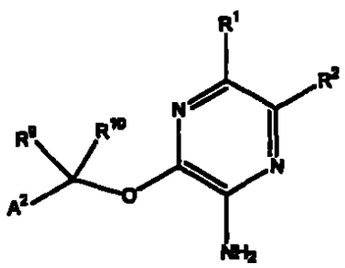
m is 0, 1 or 2;

n is 0, 1, 2, 3 or 4; and

p is 1 or 2;

or a pharmaceutically acceptable salt, solvate or hydrate thereof.

In a particular aspect of this embodiment, the compound has formula 3a



3a

wherein A^2 is C_{6-12} aryl or 5-12 membered heteroaryl optionally substituted by one or more R^3 groups.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment, R^1 is selected from C_{6-12} aryl and 5-12 membered heteroaryl, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment not inconsistent with the following definition of R^1, R^1 is selected from C_{3-12} cycloalkyl, 3-12 membered heterocalicyclic, $-O(CR^6R^7)_mR^4$, $-C(O)R^4$, $-C(O)OR^4$, $-CN$, $-NO_2$, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-C(O)NR^4R^5$, $-NR^4C(O)R^5$, $-C(=NR^6)NR^4R^5$, C_{1-8} alkyl, C_{2-8} alkenyl, and C_{2-8} alkynyl; and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment, A^2 is substituted by at least one halogen atom.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment, R^2 is hydrogen, R^9 and R^{10} are independently C_{1-4} alkyl, and A^2 is phenyl substituted by at least one halogen atom.

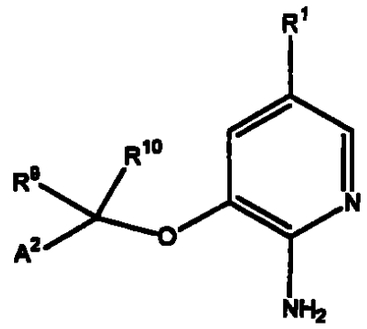
In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment not inconsistent with the following definition of R^1, R^1 is a furan, thiopene, pyrrole, pyrroline, pyrrolidine, dioxolane, oxazole, thiazole, imidazole, imidazoline, imidazolidine, pyrazole, pyrazoline, pyrazolidine, isoxazole, isothiazole, oxadiazole, triazole, thiadiazole, pyran, pyridine, piperidine, dioxane, morpholine, dithiane, thiomorpholine, pyridazine, pyrimidine, pyrazine, piperazine, triazine, trithiane or phenyl group, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment not inconsistent with the following definition of R^1, R^1 is a furan, thiopene, pyrrole, pyrroline, pyrrolidine, dioxolane, oxazole, thiazole, imidazole, imidazoline, imidazolidine, pyrazole, pyrazoline, pyrazolidine, isoxazole, isothiazole, oxadiazole, triazole, thiadiazole, pyran, pyridine, piperidine, dioxane, morpholine, dithiane, thiomorpholine, pyridazine, pyrimidine, pyrazine, triazine, trithiane or phenyl group, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups. In still more particular aspects, R^1 is not heterocalicyclic.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment not inconsistent with the following definition of R^1, R^1 is a fused ring heteroaryl group, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

In particular aspects of this embodiment, and in combination with any other particular aspects of this embodiment not inconsistent with the following definition of R^1, R^1 is a $-SO_2NR^4R^5$ group.

In another embodiment, the invention provides a compound of formula 4



4

wherein:

R^1 is selected from C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl, 3-12 membered heterocalicyclic, $-O(CR^6R^7)_nR^4$, $-C(O)R^4$, $-C(O)OR^4$, -CN, $-NO_2$, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-C(O)NR^4R^5$, $-NR^4C(O)R^5$, $-C(=NR^5)NR^4R^5$, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl; and each hydrogen in R^1 is optionally substituted by one or more R^3 groups;

R^3 is halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-O(CR^6R^7)_nR^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-C(=NR^5)NR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$, each hydrogen in R^3 is optionally substituted by one or more R^8 groups, and R^3 groups on adjacent atoms may combine to form a C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heterocalicyclic group;

each R^4, R^5, R^6 and R^7 is independently hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl; or any two of R^4, R^5, R^6 and R^7 bound to the same nitrogen atom may, together with the nitrogen to which they are bound, be combined to form a 3 to 12 membered heterocalicyclic or 5-12 membered heteroaryl group optionally containing 1 to 3 additional heteroatoms selected from N, O, and S; or any two of R^4, R^5, R^6 and R^7 bound to the same carbon atom may be combined to form a C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic or 5-12 membered heteroaryl group; and each hydrogen in R^4, R^5, R^6 and R^7 is optionally substituted by one or more R^8 groups;

each R^8 is independently halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, -CN, $-O-C_{1-12}$ alkyl, $-O-(CH_2)_nC_{3-12}$ cycloalkyl, $-O-(CH_2)_nC_{6-12}$ aryl, $-O-(CH_2)_n$(3-12 membered heterocalicyclic) or $-O-(CH_2)_n$(5-12 membered heteroaryl); and each hydrogen in R^8 is optionally substituted by one or more R^{11} groups;

each R^9 and R^{10} is independently hydrogen, halogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$; R^9 and R^{10} may combine to form a C_{3-12} cycloalkyl, 3-12 membered heterocalicyclic, C_{6-12} aryl or 5-12 membered heteroaryl ring; and each hydrogen in R^9 and R^{10} is optionally substituted by one or more R^3 groups;

A^2 is C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heterocalicyclic, and A^2 is optionally substituted by one or more R^3 groups;

each R^{11} is independently halogen, C_{1-12} alkyl, C_{1-12} alkoxy, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, -O-C_{1-12} alkyl, -O-$(CH_2)_nC_{3-12}$ cycloalkyl, -O-$(CH_2)_nC_{6-12}$ aryl, -O-$(CH_2)_n$(3-12 membered heteroalicyclic), -O-$(CH_2)_n$(5-12 membered heteroaryl) or -CN, and each hydrogen in R^{11} is optionally substituted by one or more groups selected from halogen, -OH, -CN, -C_{1-12} alkyl which may be partially or fully halogenated, -O-C_{1-12} alkyl which may be partially or fully halogenated, -CO, -SO and -SO_2;

m is 0, 1 or 2;

n is 0, 1, 2, 3 or 4; and

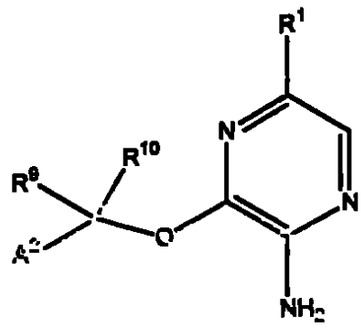
p is 1 or 2;

or a pharmaceutically acceptable salt, solvate or hydrate thereof.

In a particular aspect of this embodiment, A^2 is C_{6-12} aryl or 5-12 membered heteroaryl optionally substituted by one or more R^3 groups.

In other particular aspects of this embodiment, preferred substituents and groups of substituents include those defined in particular aspects of the previous embodiments.

In another embodiment, this invention provides a compound of formula 5



5

wherein:

R^1 is selected from C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl, 3-12 membered heteroalicyclic, -$O(CR^6R^7)_nR^4$, -$C(O)R^4$, -$C(O)OR^4$, -CN, -NO_2, -$S(O)_mR^4$, -$SO_2NR^4R^5$, -$C(O)NR^4R^5$, -$NR^4C(O)R^5$, -$C(=NR^5)NR^4R^5$, C_{1-8} alkyl, C_{2-8} alkenyl, and C_{2-8} alkynyl; and each hydrogen in R^1 is optionally substituted by one or more R^3 groups;

R^3 is halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, -$S(O)_mR^4$, -$SO_2NR^4R^5$, -$S(O)_2OR^4$, -NO_2, -NR^4R^5, -$(CR^6R^7)_nOR^4$, -CN, -$C(O)R^4$, -$OC(O)R^4$, -$O(CR^6R^7)_nR^4$, -$NR^4C(O)R^5$, -$(CR^6R^7)_nC(O)OR^4$, -$(CR^6R^7)_nNCR^4R^5$, -$C(=NR^5)NR^4R^5$, -$NR^4C(O)NR^5R^6$, -$NR^4S(O)_pR^5$ or -$C(O)NR^4R^5$, each hydrogen in R^3 is optionally substituted by one or more R^8 groups, and R^3 groups on adjacent atoms may combine to form a C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heteroalicyclic group;

each R^4, R^5, R^6 and R^7 is independently hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl; or any two of R^4, R^5, R^6 and R^7 bound to the same nitrogen atom may, together with the nitrogen to which they are bound, be combined to form a 3 to 12 membered heteroalicyclic or 5-12 membered heteroaryl group optionally containing 1 to 3 additional heteroatoms selected from N, O, and S; or any two of R^4, R^5, R^6

and R^7 bound to the same carbon atom may be combined to form a C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic or 5-12 membered heteroaryl group; and each hydrogen in R^4, R^5, R^6 and R^7 is optionally substituted by one or more R^8 groups;

each R^8 is independently halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, -CN, -O-C_{1-12} alkyl, -O-$(CH_2)_nC_{3-12}$ cycloalkyl, -O-$(CH_2)_nC_{6-12}$ aryl, -O-$(CH_2)_n$(3-12 membered heterocalicyclic) or -O-$(CH_2)_n$(5-12 membered heteroaryl); and each hydrogen in R^8 is optionally substituted by one or more R^{11} groups;

each R^9 and R^{10} is independently hydrogen, halogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$; R^9 and R^{10} may combine to form a C_{3-12} cycloalkyl, 3-12 membered heterocalicyclic, C_{6-12} aryl or 5-12 membered heteroaryl ring; and each hydrogen in R^9 and R^{10} is optionally substituted by one or more R^3 groups;

A^2 is C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heterocalicyclic, and A^2 is optionally substituted by one or more R^3 groups; except that when R^2, R^3 and R^{10} are all H and A^2 is *m*-chlorophenyl, R^1 is not unsubstituted piperazine;

each R^{11} is independently halogen, C_{1-12} alkyl, C_{1-12} alkoxy, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, -O-C_{1-12} alkyl, -O-$(CH_2)_nC_{3-12}$ cycloalkyl, -O-$(CH_2)_nC_{6-12}$ aryl, -O-$(CH_2)_n$(3-12 membered heterocalicyclic), -O-$(CH_2)_n$(5-12 membered heteroaryl) or -CN, and each hydrogen in R^{11} is optionally substituted by one or more groups selected from halogen, -OH, -CN, -C_{1-12} alkyl which may be partially or fully halogenated, -O-C_{1-12} alkyl which may be partially or fully halogenated, -CO, -SO and $-SO_2$;

m is 0, 1 or 2;

n is 0, 1, 2, 3 or 4; and

p is 1 or 2;

or a pharmaceutically acceptable salt, solvate or hydrate thereof.

In a particular aspect of this embodiment, A^2 is C_{6-12} aryl or 5-12 membered heteroaryl optionally substituted by one or more R^3 groups.

In other particular aspects of this embodiment, preferred substituents and groups of substituents include those defined in particular aspects of the previous embodiments.

In another embodiment, the invention provides a compound selected from the group consisting of: 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenol; 3-(2,6-dichloro-benzyloxy)-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-[3-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(1H-indol-4-yl)-pyridin-2-ylamine; 3-[2-chloro-6-(1H-indol-4-yl)-benzyloxy]-5-(1H-indol-4-yl)-pyridin-2-ylamine; 2-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-pyrrole-1-carboxylic acid tert-butyl ester; 3-(2,6-dichloro-benzyloxy)-5-(1H-pyrrol-2-yl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(4-fluoro-phenyl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(2-fluoro-phenyl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(3-fluoro-phenyl)-pyridin-2-ylamine; 5-(4-amino-phenyl)-3-(2,6-

dichloro-benzyloxy)-pyridin-2-ylamine; *N*-{4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-methanesulfonamide; N-{4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-acetamide; 3-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenol; 3-(2,6-dichloro-benzyloxy)-5-(4-methoxy-phenyl)-pyridin-2-ylamine; 5-(3-amino-phenyl)-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(3-trifluoromethoxy-phenyl)-pyridin-2-ylamine; 2-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenol; 3-(2,6-dichloro-benzyloxy)-5-(2-phenoxy-phenyl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(3,4-difluoro-phenyl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(3-isopropyl-phenyl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(2-trifluoromethyl-phenyl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(2-methoxy-phenyl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(4-trifluoromethyl-phenyl)-pyridin-2-ylamine; *N*-{2-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-methanesulfonamide; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-methanol; 5-benzo[1,3]dioxol-5-yl-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(2-trifluoromethoxy-phenyl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(4-methyl-thiophen-2-yl)-pyridin-2-ylamine; 5-(2-benzyloxy-phenyl)-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(3-methoxy-phenyl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(1*H*-indol-2-yl)-pyridin-2-ylamine; 5-(4-benzyloxy-3-fluoro-phenyl)-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine; 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid; 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-N-(2-diethylamino-ethyl)-benzamide; 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-N-(3-diethylamino-propyl)-benzamide; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[4-(2-hydroxy-ethyl)-piperidin-1-yl]-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*R*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-cyclopropylaminomethyl-piperidin-1-yl]-methanone; 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-*N*-(2-hydroxy-3-pyrrolidin-1-yl-propyl)-benzamide; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-(3-fluoro-piperidin-1-ylmethyl)-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-cyclopropyl-piperazin-1-yl)-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-{(2R)-2-[(cyclopropylmethyl-amino)-methyl]-pyrrolidin-1-yl}-methanone; 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-N-cyclopropylmethyl-*N*-(2*R*)-pyrrolidin-2-ylmethyl-benzamide; 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-N-(2-hydroxy-3-pyrrolidin-1-yl-propyl)-N-methyl-benzamide; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-{(2*S*)-2-[(3*R*)-3-hydroxy-pyrrolidin-1-ylmethyl]-pyrrolidin-1-yl}-methanone; 3-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid; {3-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenoxy}-acetic acid; 2-{4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenoxy}-1-[(2R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-ethanone;

2-{4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenoxy}-1-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-ethanone; 3-(2,6-dichloro-benzyloxy)-5-(1H-indol-5-yl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-[3-(1-methyl-1,2,3,6-tetrahydro-pyridin-4-yl)-1H-indol-5-yl]-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-[3-(1-methyl-piperidin-4-yl)-1*H*-indol-5-yl]-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(3-morpholin-4-ylmethyl-1*H*-indol-5-yl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(3-piperidin-1-ylmethyl-1*H*-indol-5-yl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(3-pyrrolidin-1-ylmethyl-1*H*-indol-5-yl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(3-diethylaminomethyl-1H-indol-5-yl)-pyridin-2-ylamine; (1-{5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-3-ylmethyl}-(3*R*)-pyrrolidin-3-yl)-carbamic acid *tert*-butyl ester; 3-(2,6-dichloro-benzyloxy)-5-[3-(2,6-dimethyl-morpholin-4-ylmethyl)-1*H*-indol-5-yl]-pyridin-2-ylamine; *N*-(1-{5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-3-ylmethyl}-(3*R*)-pyrrolidin-3-yl)-acetamide; 1-(4-{5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-3-ylmethyl}-piperazin-1-yl)-ethanone; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(1*H*-indol-5-yl)-pyridin-2-ylamine; 1-(4-{5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-1*H*-indol-3-ylmethyl}-piperazin-1-yl)-ethanone; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-[3-(2,6-dimethyl-morpholin-4-ylmethyl)-1*H*-indol-5-yl]-pyridin-2-ylamine; *N*-(1-{5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-1*H*-indol-3-ylmethyl}-(3*S*)-pyrrolidin-3-yl)-acetamide; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(3-piperidin-1-ylmethyl-1*H*-indol-5-yl)-pyridin-2-ylamine; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(3-morpholin-4-ylmethyl-1*H*-indol-5-yl)-pyridin-2-ylamine; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(3-pyrrolidin-1-ylmethyl-1*H*-indol-5-yl)-pyridin-2-ylamine; 5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carboxylic acid ethyl ester; 5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carboxylic acid; {5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-2-yl}-(4-methyl-piperazin-1-yl)-methanone; {5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-2-yl}-[(3*R*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-2-yl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; 5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carboxylic acid (2-pyrrolidin-1-yl-ethyl)-amide; 5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carboxylic acid (2-morpholin-4-yl-ethyl)-amide; (1-{5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carbonyl}-(3*S*)-pyrrolidin-3-yl)-carbamic acid *tert*-butyl ester; {5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-2-yl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone; 5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carboxylic acid (2-hydroxy-3-pyrrolidin-1-yl-propyl)-amide; 4-(6-amino-5-benzyloxy-pyridin-3-yl)-phenol; 3-benzyloxy-5-phenyl-pyridin-2-ylamine; 3-(3-methoxy-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2-chloro-4-fluoro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2-chloro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2,5-dichloro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2-chloro-5-trifluoromethyl-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2,4-dichloro-5-fluoro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2-chloro-3-trifluoromethyl-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(3,4-dichloro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 2-(2-amino-5-phenyl-pyridin-3-yloxymethyl)-benzonitrile; 3-(2-chloro-6-fluoro-3-methyl-benzyloxy)-5-phenyl-pyridin-2-ylamine; 5-Phenyl-3-(2,3,6-trifluoro-benzyloxy)-pyridin-2-ylamine; 3-(2,6-difluoro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2,6-difluoro-3-methyl-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(3-chloro-2,6-difluoro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2-chloro-6-fluoro-benzyloxy)-

5-phenyl-pyridin-2-ylamine; 3-(3-Fluoro-4-methoxy-benzyloxy)-5-phenyl-pyridin-2-ylamine; *N*-[3-(2-amino-5-phenyl-pyridin-3-yloxymethyl)-phenyl]-methanesulfonamide; 5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-3-(3-nitro-benzyloxy)-pyridin-2-ylamine; 5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-3-(naphthalen-1-ylmethoxy)-pyridin-2-ylamine; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 2-[2-amino-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-3-yloxy]-*N*-(4-isopropyl-phenyl)-2-phenyl-acetamide; 3-(5-chloro-benzo[*b*]thiophen-3-ylmethoxy)-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine; {4-[6-amino-5-(4-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-fluoro-6-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(5-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; (4-[6-amino-5-[1-(2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-bromo-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; 4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenol; 3-(2,6-difluoro-benzyloxy)-5-(1H-indol-4-yl)-pyridin-2-ylamine; 3-(2,6-difluoro-benzyloxy)-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid; {4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenoxy}-acetic acid ethyl ester; {4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenoxy}-acetic acid; 2-{4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenoxy}-1-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-ethanone; 2-{4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenoxy}-1-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-ethanone; 4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-phenol; 4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-phenol; 4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenol; 2-[2-amino-5-(4-hydroxy-phenyl)-pyridin-3-yloxymethyl]-benzonitrile; 4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenol; 4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenol; 4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-phenol; *N*-(4-[6-amino-5-(2-cyano-benzyloxy)-pyridin-3-yl]-phenyl}-methanesulfonamide; 2-[2-amino-5-(4-methanesulfonylamino-phenyl)-pyridin-3-yloxymethyl]-benzamide; 2-[2-amino-5-(4-methanesulfonylamino-phenyl)-pyridin-3-yloxymethyl]-benzoic acid; *N*-(4-[6-amino-5-[2-(4-methyl-piperazine-1-carbonyl)-benzyloxy]-pyridin-3-yl}-phenyl)-methanesulfonamide; 2-[2-amino-5-(4-methanesulfonylamino-phenyl)-pyridin-3-yloxymethyl]-*N*-(2-hydroxy-ethyl)-benzamide; 2-[2-amino-5-(4-methanesulfonylamino-phenyl)-pyridin-3-yloxymethyl]-*N*-isobutyl-benzamide; 4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-benzoic acid; {4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone;

{4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; 1-(4-{4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-benzoyl}-piperazin-1-yl)-ethanone; 4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; 4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-benzoic acid; {4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; 1-(4-{4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-benzoyl}-piperazin-1-yl)-ethanone; 4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; 4-[6-amino-5-(2-cyano-benzyloxy)-pyridin-3-yl]-benzoic acid; 2-{2-amino-5-[4-((2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl}-benzonitrile; 2-{2-amino-5-[4-((2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl}-benzonitrile; 2-{2-amino-5-[4-((3*S*)-3-dimethylamino-pyrrolidine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl}-benzonitrile; 2-{2-amino-5-[4-((3*S*)-3-amino-pyrrolidine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl}-benzonitrile; 2-{2-amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl}-benzonitrile; 2-{2-amino-5-[4-(4-methyl-piperazine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl}-benzonitrile; 2-{5-[4-(4-acetyl-piperazine-1-carbonyl)-phenyl]-2-amino-pyridin-3-yloxymethyl}-benzonitrile; 4-[6-amino-5-(2-cyano-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; 4-[6-amino-5-(2-cyano-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 4-[6-amino-5-(2-cyano-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; 4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid; {4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; 1-(4-{4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-benzoyl}-piperazin-1-yl)-ethanone; 4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; 4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; 4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-benzoic acid; {4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(3S)-3-dimethylamino-pyrrolidin-1-yl]-methanone; [(3*S*)-3-amino-pyrrolidin-1-yl]-{4-[6-amino-

93

5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-methanone; {4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; 1-(4-[4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-benzoyl}-piperazin-1-yl)-ethanone; 4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; 4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; 4-[6-amino-5-(4-tert-butyl-benzyloxy)-pyridin-3-yl]-benzoic acid; {4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(3R)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; 1-(4-{4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-benzoyl}-piperazin-1-yl)-ethanone; 4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; 4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; 4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-benzoic acid; {4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3S)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; 1-(4-{4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-benzoyl}-piperazin-1-yl)-ethanone; 4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid; {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-amino-piperidin-1-yl)-methanone; {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone; {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3S)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*R*)-3-amino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone; 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(2-pyrrolidin-1-yl-ethyl)-benzamide; 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(3-pyrrolidin-1-yl-propyl)-benzamide; 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; 3-[6-amino-5-(2-

chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid; {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-amino-piperidin-1-yl)-methanone; {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone; {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*R*)-3-amino-pyrrolidin-1-yl]-methanone; {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-amino-pyrrolidin-1-yl]-methanone; 3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; 3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(2-pyrrolidin-1-yl-ethyl)-benzamide; 3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(3-pyrrolidin-1-yl-propyl)-benzamide; 3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; *N*-[2-(4-acetyl-piperazin-1-yl)-ethyl]-3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzamide; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-[4-(1,1-dioxo-1λ^6-isothiazolidin-2-yl)-phenyl]-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-[4-(1,1-dioxo-1λ^6-isothiazolidin-2-yl)-phenyl]-pyridin-2-ylamine; 5-[4-(1,1-dioxo-1λ^6-isothiazolidin-2-yl)-phenyl]-3-(2-fluoro-6-trifluoromethyl-benzyloxy)-pyridin-2-ylamine; 2-diethylamino-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-cyclopropylamino-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-Pyrrolidin-1-yl-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-(4-hydroxy-piperidin-1-yl)-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-morpholin-4-yl-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-Piperidin-1-yl-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-dimethylamino-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-(4-acetyl-piperazin-1-yl)-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-(cyclopropylmethyl-amino)-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-[(3*R*)-3-hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-[(2S)-2-hydroxymethyl-pyrrolidin-1-yl]-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-[4-(2-hydroxy-acetyl)-piperazin-1-yl]-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-(4-acetyl-piperazin-1-yl)-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-Pyrrolidin-1-yl-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-morpholin-4-yl-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-diethylamino-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-dimethylamino-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-Piperidin-1-yl-ethanesulfonic acid {3-[6-

amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-[(3*R*)-3-hydroxymethyl-pyrrolidin-1-yl]-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-(4-hydroxy-piperidin-1-yl)-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-[4-(2-hydroxy-acetyl)-piperazin-1-yl]-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-[(3*R*)-3-hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-(cyclopropylmethyl-amino)-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-cyclopropylamino-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(2-dimethylaminomethyl-phenyl)-pyridin-2-ylamine; compound with trifluoro-acetic acid; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(3-pyrrolidin-1-yl-phenyl)-pyridin-2-ylamine; compound with trifluoro-acetic acid; *N*-{4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-methanesulfonamide; compound with trifluoro-acetic acid; 5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophene-2-carboxylic acid; {5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophen-2-yl}-(4-methyl-piperazin-1-yl)-methanone; {5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophen-2-yl}-[(2R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; 5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophene-2-carboxylic acid (1-methyl-piperidin-4-yl)-amide; {5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophen-2-yl}-(3,5-dimethyl-piperazin-1-yl)-methanone; 5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophene-2-carboxylic acid (2-pyrrolidin-1-yl-ethyl)-amide; {5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophen-2-yl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-benzoic acid; {4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; {4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone; {4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-(3-dimethylamino-pyrrolidin-1-yl)-methanone; {4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; 4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; {4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; *N*-[2-(4-acetyl-piperazin-1-yl)-ethyl]-4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-benzamide; 2-Piperidin-1-yl-ethanesulfonic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 2-(4-hydroxy-piperidin-1-yl)-ethanesulfonic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 2-dimethylamino-ethanesulfonic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 2-cyclopropylamino-ethanesulfonic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-benzoic acid; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-[(2R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; 4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-*N*-(1-methyl-piperidin-4-yl)-benzamide; (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-[(3*R*)-3-amino-pyrrolidin-1-yl)]-methanone;

(4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(3,5-dimethyl-piperazin-1-yl)-methanone; 2-cyclopropylamino-ethanesulfonic acid (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 2-dimethylamino-ethanesulfonic acid (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 2-[(3*R*)-3-hydroxy-pyrrolidin-1-yl)]-ethanesulfonic acid (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy)-pyridin-3-yl}-phenyl)-amide; and pharmaceutically acceptable salts, hydrates and solvates thereof.

In another embodiment, the invention provides a compound selected from the group consisting of: 4-[6-amino-6-(2,6-dichloro-benzyloxy)-pyrazin-2-yl]-phenol; 3-(2,6-dichloro-benzyloxy)-5-[4-(1,1-dioxo-1λ^6-isothiazolidin-2-yl)-phenyl]-pyrazin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-[3-(2-morpholin-4-yl-ethoxy)-phenyl]-pyrazin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyrazin-2-ylamine; 5-(4-amino-phenyl)-3-(2,6-dichloro-benzyloxy)-pyrazin-2-ylamine; 4-[5-amino-6-(2,6-dichloro-benzyloxy)-pyrazin-2-yl]-benzoic acid; {4-[5-amino-6-(2,6-dichloro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[5-amino-6-(2,6-dichloro-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 2-morpholin-4-yl-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-piperidin-1-yl-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-pyrrolidin-1-yl-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-[(3*R*)-3-Hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-[(2*S*)-2-Hydroxymethyl-pyrrolidin-1-yl]-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-(cyclopropylmethyl-amino)-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-dimethylamino-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-diethylamino-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-(4-acetyl-piperazin-1-yl)-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-[4-(2-Hydroxy-acetyl)-piperazin-1-yl]-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-cyclopropylamino-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-[(3*R*)-3-Hydroxymethyl-pyrrolidin-1-yl]-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-(4-acetyl-piperazin-1-yl)-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-piperidin-1-yl-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-diethylamino-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-morpholin-4-yl-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-pyrrolidin-1-yl-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-dimethylamino-ethanesulfonic acid {3-[5-amino-6-(2-chloro-

3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-[4-(2-Hydroxy-acetyl)-piperazin-1-yl]-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-(cyclopropylmethyl-amino)-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-[(3*R*)-3-Hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-cyclopropylamino-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-benzoic acid; {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; 4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(2-pyrrolidin-1-yl-ethyl)-benzamide; {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone; *N*-[2-(4-acetyl-piperazin-1-yl)-ethyl]-4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-benzamide; 4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(3-pyrrolidin-1-yl-propyl)-benzamide; {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(3*R*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone; {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; 4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; 4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; 3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-benzoic acid; {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(3*R*)-3-amino-pyrrolidin-1-yl]-methanone; {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone; {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone; 3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; 3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(2-pyrrolidin-1-yl-ethyl)-benzamide; 3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(2*S*)-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; 3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; *N*-[2-(4-acetyl-piperazin-1-yl)-ethyl]-3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-benzamide; 3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(3-pyrrolidin-1-yl-propyl)-benzamide; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(1*H*-indol-5-yl)-pyrazin-2-ylamine; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(3-pyrrolidin-1-ylmethyl-1*H*-indol-5-yl)-pyrazin-2-ylamine; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(3-diethylaminomethyl-1*H*-indol-5-yl)-pyrazin-2-ylamine; 1-(4-{5-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-1*H*-indol-3-ylmethyl}-piperazin-1-yl)-ethanone; 3-(2-chloro-3,6-difluoro-

benzyloxy)-5-[3-(2,6-dimethyl-morpholin-4-ylmethyl)-1*H*-indol-5-yl]-pyrazin-2-ylamine; *N*-(1-{5-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-1*H*-indol-3-ylmethyl}-(3*S*)-pyrrolidin-3-yl)-acetamide; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(3-piperidin-1-ylmethyl-1*H*-indol-5-yl)-pyrazin-2-ylamine; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(3-morpholin-4-ylmethyl-1*H*-indol-5-yl)-pyrazin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-2-methyl-propoxy]-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyrazin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyrazin-2-ylamine; compound with trifluoro-acetic acid; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyrazin-2-ylamine; compound with trifluoro-acetic acid; *N*-(4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-methanesulfonamide; 2-pyrrolidin-1-yl-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-piperidin-1-yl-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-(cyclopropylmethyl-amino)-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-[(3*R*)-3-Hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-[(2*S*)-2-Hydroxymethyl-pyrrolidin-1-yl]-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-dimethylamino-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-morpholin-4-yl-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-diethylamino-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-cyclopropylamino-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-benzoic acid; (3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone; (3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-[(3*R*)-3-amino-pyrrolidin-1-yl]-methanone; (3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; *N*-[2-(4-acetyl-piperazin-1-yl)-ethyl]-3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-benzamide; (3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; 3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-benzoic acid; 3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-*N*-(1-methyl-piperidin-4-yl)-benzamide; 3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-*N*-(3-pyrrolidin-1-yl-propyl)-benzamide; (3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 4-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-benzoic acid; 4-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 4-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; and pharmaceutically acceptable salts, hydrates and solvates thereof.

In another embodiment, the invention provides a compound selected from the group consisting of: (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; *N*-[2-(4-acetyl-piperazin-1-yl)-ethyl]-4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-

pyridin-3-yl]-benzamide; 4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide; 4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-amino-piperidin-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-3-hydroxy-pyrrolidin-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-3-hydroxy-pyrrolidin-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-2-hydroxymethyl-pyrrolidin-1-yl)-methanone; 4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-diethylamino-ethyl)-benzamide; 4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; 3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid; (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone; 3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(1-methyl-piperidin-4-yl)-benzamide; (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; N-[2-(4-acetyl-piperazin-1-yl)-ethyl]-3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzamide; (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone; 3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(3-morpholin-4-yl-propyl)-benzamide; (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; 3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; 3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide; 3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide; (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 2-diethylamino-ethanesulfonic acid (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide; 2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide; 2-piperidin-1-yl-ethanesulfonic acid (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide; 2-(cyclopropylmethyl-amino)-ethanesulfonic acid (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide; 2-((R)-3-Hydroxy-pyrrolidin-1-yl)-ethanesulfonic acid (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide; 2-cyclopropylamino-ethanesulfonic acid (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide; 2-diethylamino-ethanesulfonic acid (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide; 4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid; 4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide; 4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(1-methyl-piperidin-4-yl)-benzamide; (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone; (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-

3-yl]-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide; (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone; 3-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid; (3-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; (3-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone; 3-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(1-methyl-piperidin-4-yl)-benzamide; (3-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone; 3-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide; 3-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; (3-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone; 3-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide; (3-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (3-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-[3-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-[2-(1-methyl-pyrrolidin-2-yl)-ethoxy]-phenyl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[3-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 1-(4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenoxy)-3-morpholin-4-yl-propan-2-ol; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(2-diethylamino-ethoxy)-phenyl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(1-methyl-piperidin-3-ylmethoxy)-phenyl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(2-diisopropylamino-ethoxy)-phenyl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(1-methyl-piperidin-4-yloxy)-phenyl]-pyridin-2-ylamine; N-(4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-methanesulfonamide; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-[4-(1,1-dioxo-1lambda*6*-isothiazolidin-2-yl)-phenyl]-pyridin-2-ylamine; N-(4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-methanesulfonamide; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-phenyl-pyridin-2-ylamine; N-(4-[6-amino-5-[(R)-1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-methanesulfonamide; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-thiophen-3-yl-pyridin-2-ylamine; 5-benzo[b]thiophen-2-yl-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 4-methyl-piperazine-1-carboxylic acid (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide; 1-(4-[6-amino-5-[1-(2,6-

dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(2-pyrrolidin-1-yl-ethyl)-urea; 1-(4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(2-hydroxy-ethyl)-urea; 1-(4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(2-morpholin-4-yl-ethyl)-urea; (R)-3-amino-pyrrolidine-1-carboxylic acid (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; (S)-3-amino-pyrrolidine-1-carboxylic acid (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 1-(4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(1-methyl-piperidin-4-yl)-urea; 1-(4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(1-methyl-piperidin-4-yl)-urea; (R)-3-amino-pyrrolidine-1-carboxylic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; (S)-3-amino-pyrrolidine-1-carboxylic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 1-(4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(2-hydroxy-ethyl)-urea; 4-methyl-piperazine-1-carboxylic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 1-(4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(2-pyrrolidin-1-yl-ethyl)-urea; 1-(4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(2-morpholin-4-yl-ethyl)-urea; (R)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-benzoic acid; (3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; (3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; 3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; (3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; 3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide; N-[2-(4-acetyl-piperazin-1-yl)-ethyl]-3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-benzamide; 3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; (3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone; (3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone; 4-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-benzoic acid; 4-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; 4-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; (4-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; 4-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; (4-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; N-[2-(4-acetyl-piperazin-1-yl)-ethyl]-4-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-benzamide; 4-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide; (4-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((S)-3-aminopyrrolidin-1-yl)-methanone; (4-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-

phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone; (4-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (4-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; (4-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (S)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-amide; 4-methyl-piperazine-1-carboxylic acid (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-amide; 4-pyrrolidin-1-yl-piperidine-1-carboxylic acid (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-amide; (3R,5S)-3,5-dimethyl-piperazine-1-carboxylic acid (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-amide; 1-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-3-(1-methyl-piperidin-4-yl)-urea; 1-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-3-(3-pyrrolidin-1-yl-propyl)-urea; 1-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-3-(2-pyrrolidin-1-yl-ethyl)-urea; 1-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-3-(2-morpholin-4-yl-ethyl)-urea; 1-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-3-(3-morpholin-4-yl-propyl)-urea; (R)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-amide; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-dimethylamino-prop-1-ynyl)-pyridin-2-ylamine; (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-urea; N-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-2-piperidin-1-yl-acetamide; N-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-2-morpholin-4-yl-acetamide; N-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-2-pyrrolidin-1-yl-acetamide; N-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-2-((R)-3-hydroxy-pyrrolidin-1-yl)-acetamide; N-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-2-(4-hydroxy-piperidin-1-yl)-acetamide; N-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-2-dimethylamino-acetamide; N-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-2-diethylamino-acetamide; 2-(4-acetyl-piperazin-1-yl)-N-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]pyridin-3-yl}-prop-2-ynyl)-acetamide; 4-methyl-piperazine-1-carboxylic acid (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-1,1-dimethyl-prop-2-ynyl)-amide; (3R,5S)-3,5-dimethyl-piperazine-1-carboxylic acid (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-1,1-dimethyl-prop-2-ynyl)-amide; (R)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-1,1-dimethyl-prop-2-ynyl)-amide; (S)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-1,1-dimethyl-prop-2-ynyl)-amide; 1-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-1,1-dimethyl-prop-2-ynyl)-3-(2-morpholin-4-yl-ethyl)-urea; 1-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-1,1-dimethyl-prop-2-ynyl)-3-(2-pyrrolidin-1-yl-ethyl)-urea; 4-pyrrolidin-1-yl-piperidine-1-carboxylic acid (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-1,1-dimethyl-prop-2-ynyl)-amide; 3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-propynoic acid cyclohexylamide; 3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-propynoic acid isopropylamide; 4-(3-

amino-3-methyl-but-1-ynyl)-2-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-phenylamine; (4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1yl)-methanone; (4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; (4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; 4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; 4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; 4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; 4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide; 4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-N-(3-morpholin-4-yl-propyl)-benzamide; 6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-nicotinonitrile; 6-amino-5-[1-(2,6-dichloro-3-cyano-phenyl)-ethoxy]-nicotinonitrile; 5-aminomethyl-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; (R)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid {6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-ylmethyl}-amide; N-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-ylmethyl}-methanesulfonamide; N-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-ylmethyl}-acetamide; N-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-ylmethyl}-4-methyl-benzenesulfonamide; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-vinyl-pyridin-2-ylamine; (S)-1-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-ethane-1,2-diol; (R)-1-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-ethane-1,2-diol; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(1H-pyrazol-4-yl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[1-(2-pyrrolidin-1-yl-ethyl)-1H-pyrazol-4-yl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[1-(2-diisopropylamino-ethyl)-1H-pyrazol-4-yl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[1-(2-morpholin-4-yl-ethyl)-1H-pyrazol-4-yl]-pyridin-2-ylamine; 5-bromo-3-(3-fluoro-2-methoxy-benzyloxy)-pyridin-2-ylamine; 5-bromo-3-[1-(3-fluoro-2-methoxy-phenyl)-ethoxy]-pyridin-2-ylamine; {4-[6-amino-5-(3-fluoro-2-methoxy-benzyloxy)-pyridin-3-yl]-phenyl}-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; (4-{6-amino-5-[1-(3-fluoro-2-methoxy-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 5-bromo-3-(3-fluoro-2-isopropoxy-benzyloxy)-pyridin-2-ylamine; {4-[6-amino-5-(3-fluoro-2-isopropoxy-benzyloxy)-pyridin-3-yl]-phenyl}-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 5-(4-amino-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenoxy)-acetic acid methyl ester; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenoxy)-acetic acid; 2-(4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenoxy)-1-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-ethanone; 2-(4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenoxy)-1-((R)-3-hydroxy-pyrrolidin-1-yl)-ethanone; 4-[2-(4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenoxy)-acetyl]-piperazine-1-carboxylic acid tert-butyl ester; 2-(4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenoxy)-1-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-ethanone; 5-bromo-3-(3-fluoro-6,7,8,9-

tetrahydro-5*H*-benzocyclohepten-5-yloxy)-pyridin-2-ylamine; {4-[6-amino-5-(3-fluoro-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-yloxy)-pyridin-3-yl]-phenyl}-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 3-(3-fluoro-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-yloxy)-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-pyridin-2-ylamine; N-{4-[6-amino-5-(3-fluoro-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-yloxy)-pyridin-3-yl]-phenyl}-methanesulfonamide; 3-(3-fluoro-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-yloxy)-5-(1H-pyrazol-4-yl)-pyridin-2-ylamine; 5-bromo-3-[1-(2-chloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 3-[1-(2-chloro-3-fluoro-phenyl)-ethoxy]-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 5'-benzyloxy-[2,3']bipyridinyl-6'-ylamine; 5-benzyloxy-[3,3']bipyridinyl-6-ylamine; 3-benzyloxy-5-pyrimidin-5-yl-pyridin-2-ylamine; 5-benzyloxy-[3,3']bipyridinyl-6,6'-diamine; 5'-(2-chloro-benzyloxy)-[2,3']bipyridinyl-6'-ylamine; 5-(2-chloro-benzyloxy)-[3,3']bipyridinyl-6-ylamine; 3-(2-chloro-benzyloxy)-5-pyrimidin-5-yl-pyridin-2-ylamine; 5-(2-chloro-benzyloxy)-[3,3']bipyridinyl-6,6'-diamine; 5'-(4-chloro-benzyloxy)-[2,3']bipyridinyl-6'-ylamine; 5-(4-chloro-benzyloxy)-[3,3']bipyridinyl-6-ylamine; 3-(4-chloro-benzyloxy)-5-pyrimidin-5-yl-pyridin-2-ylamine; 5-(4-chloro-benzyloxy)-[3,3']bipyridinyl-6,6'-diamine; 5'-(2-chloro-3,6-difluoro-benzyloxy)-[2,3']bipyridinyl-6'-ylamine; 5-(2-chloro-3,6-difluoro-benzyloxy)-[3,3']bipyridinyl-6-ylamine; 5-(2-chloro-3,6-difluoro-benzyloxy)-[3,4']bipyridinyl-6-ylamine; 3-(2-chloro3,6-difluoro-benzyloxy)-5-pyrimidin-5-yl-pyridin-2-ylamine; 5-(2-chloro-3,6-difluoro-benzyloxy)-[3,3']bipyridinyl-6,6'-diamine; 5'-(2,6-dichloro-benzyloxy)-[2,3']bipyridinyl-6'-ylamine; 5-(2,6-dichloro-benzyloxy)-[3,3']bipyridinyl-6-ylamine; 5-(2,6-dichloro-benzyloxy)-[3,4']bipyridinyl-6-ylamine; 3-(2,6-dichloro-benzyloxy)-5-pyrimidin-5-yl-pyridin-2-ylamine; 5-(2,6-dichloro-benzyloxy)-[3,3']bipyridinyl-6,6'-diamine; 5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6,6'-diamine; {6'-amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-4-yl}-(4-methyl-piperazin-1-yl)-methanone; {6'-amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-6-yl}-(4-methyl-piperazin-1-yl)-methanone; {6'-amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-5-yl}-(4-methyl-piperazin-1-yl)-methanone; {6'-amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6-yl}-(4-methyl-piperazin-1-yl)-methanone; {6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[3,4']bipyridinyl-2'-yl}-(4-methyl-piperazin-1-yl)-methanone; 5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6,6'-diamine; {6'-amino-5'-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-5-yl}-(4-methyl-piperazin-1-yl)-methanone; {6'-amino-5'-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-4-yl}-(4-methyl-piperazin-1-yl)-methanone; {6'-amino-5'-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-6-yl}-(4-methyl-piperazin-1-yl)-methanone; {6'-amino-5'-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-5-yl}-(4-methyl-piperazin-1-yl)-methanone; {6'-amino-5'-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6-yl}-(4-methyl-piperazin-1-yl)-methanone; {6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[3,4']bipyridinyl-2'-yl}-(4-methyl-piperazin-1-yl)-methanone; 5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-6'-ylamine; 5'-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-6'-ylamine; 5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-pyrimidin-5-yl-pyridin-2-ylamine; {6'-amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-5-yl}-(4-methyl-piperazin-1-yl)-methanone; 5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[3,4']bipyridinyl-6-ylamine; 5-benzyloxy-3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-(2-ethyl-butoxy)-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-(3-methyl-butoxy)-

pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-butoxy-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-propoxy-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-cyclohexylmethoxy-pyridin-2-ylamine; 6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-ol; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-(2-cyclohexyl-ethoxy)-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-isobutoxy-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-phenethyloxy-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-(pyridin-2-ylmethoxy)-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-(pyridin-4-ylmethoxy)-pyridin-2-ylamine; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 5-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-2-fluoro-benzonitrile; 4-(4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-piperidin-4-ol; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-piperidin-1-yl-methanone; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-pyrrolidin-1-yl-methanone; 4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-3-methyl-benzoic acid methyl ester; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(dimethyl-piperazin-1-ylmethyl)-phenyl]-pyridin-2-ylamine; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-3,5-dimethoxy-phenyl)-(dimethyl-piperazin-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-2-fluoro-phenyl)-(dimethyl-piperazin-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-3-fluoro-phenyl)-(dimethyl-piperazin-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-3-methyl-phenyl)-(dimethyl-piperazin-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-methyl-[1,4]diazepan-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-[1,4]diazepan-1-yl-methanone; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-piperazin-1-yl-methanone; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-vinyl-pyridin-2-ylamine; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((3R,4S)-3,4-dihydroxy-pyrrolidin-1-yl)-methanone; 5-[(1-benzyl-pyrrolidin-3-ylamino)-methyl]-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-azetidin-3-yl-benzamide; 4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N,N-dimethyl-benzenesulfonamide; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(6-methoxy-1H-benzoimidazol-2-yl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(6-methoxy-1-methyl-1H-benzoimidazol-2-yl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(4-methyl-[1,4]diazepane-1-sulfonyl)-phenyl]-pyridin-2-ylamine; 6-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-1-methyl-1H-indazole-3-carboxylic acid amide; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(1-methyl-1H-pyrazol-4-yl)-pyridin-2-ylamine; 5-(3-chloro-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(4-fluoro-3-methyl-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-trifluoromethyl-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-fluoro-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-trifluoromethoxy-phenyl)-pyridin-2-ylamine; 5-benzo[1,3]dioxol-5-yl-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 3-[6-

amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenol; (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-methanol; 3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-benzonitrile; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-methoxy-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3,5-dichloro-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2,5-dimethyl-phenyl)-pyridin-2-ylamine; 5-(5-chloro-2-methoxy-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 5-(3-chloro-4-fluoro-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(5-fluoro-2-methoxy-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-isopropyl-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3,4-dichloro-phenyl)-pyridin-2-ylamine; 4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-benzonitrile; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3,4-difluoro-phenyl)-pyridin-2-ylamine; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((2R,6S)-2,6-dimethyl-morpholin-4-yl)-methanone; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2-ethoxy-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2,5-dimethoxy-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2,4-dimethoxy-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2,6-dimethoxy-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2-trifluoromethyl-phenyl)-pyridin-2-ylamine; 5-(2-chloro-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2-trifluoromethoxy-phenyl)-pyridin-2-ylamine; 1-(2-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-ethanone; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2-fluoro-phenyl)-pyridin-2-ylamine; (2-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-methanol; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-o-tolyl-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2-methoxy-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2,6-dimethyl-phenyl)-pyridin-2-ylamine; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-morpholin-4-yl-methanone; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-2-chloro-phenyl)-((3R,5S)-dimethyl-piperazin-1-yl)-methanone; 4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-2-methyl-phenyl)-((3R,5S)-dimethyl-piperazin-1-yl)-methanone; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-((2R,6S)-2,6-dimethyl-morpholin-4-ylmethyl)-phenyl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(4-morpholin-4-ylmethyl-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3,5-dimethyl-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-m-tolyl-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3,4-dimethoxy-phenyl)-pyridin-2-ylamine; 5-biphenyl-3-yl-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 5-(3,5-bis-trifluoromethyl-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3,4-dichloro-phenyl)-pyridin-2-ylamine; 1-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-ethanone; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3,5-difluoro-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2,5-dichloro-phenyl)-pyridin-2-ylamine; (4-{6-amino-5-[1-(2,6-dichloro-4-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-ethoxy-phenyl)-pyridin-2-ylamine; (4-{6-amino-5-[1-(2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-

phenyl)-(3,5-dimethyl-piperazin-1-yl)-methanone; (4-[6-amino-5-[1-(3-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(3,5-dimethyl-piperazin-1-yl)-methanone; 7-[4-(3,5-dimethyl-piperazine-1-carbonyl)-phenyl]-2-phenyl-4H-pyrido[3,2-b][1,4]oxazin-3-one; {4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone; {4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone; [4-(6-amino-5-benzyloxy-pyridin-3-yl)-phenyl]-(3,5-dimethyl-piperazin-1-yl)-methanone; (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-ethyl-piperazin-1-yl)-methanone; [4-(6-amino-5-benzyloxy-pyridin-3-yl)-phenyl]-(4-ethyl-piperazin-1-yl)-methanone; {4-[6-amino-5-(2-methyl-benzyloxy)-pyridin-3-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone; 3-[2-amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl]-benzoic acid methyl ester; 3-[2-amino-5-[4-(3,5-dimethyl-piperazine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl]-benzoic acid methyl ester; {4-[6-amino-5-(2-methyl-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; [4-(6-amino-5-cyclohexylmethoxy-pyridin-3-yl)-phenyl]-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 4-(1-{2-amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxy}-ethyl)-[2-(3-hydroxy-phenyl)-ethyl]-benzamide; 4-(1-{2-amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxy}-ethyl)-[2-(2,6-dichloro-phenyl)-ethyl]-benzamide; 4-(1-{2-amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxy}-ethyl)-(1-benzyl-piperidin-4-yl)-benzamide; 4-(1-{2-amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxy}-ethyl)-[3-(2-oxo-pyrrolidin-1-yl)-propyl]-benzamide; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-ethyl-piperazin-1-yl)-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone; (6-amino-3-aza-bicyclo[3.1.0]hex-3-yl)-(4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-methanone; 5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-6'-(2-morpholin-4-yl-ethoxy)-[3,3']bipyridinyl-6-ylamine; 6'-amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-1-(2-pyrrolidin-1-yl-ethyl)-1H-[3,3']bipyridinyl-6-one; 5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-6'-(2-pyrrolidin-1-yl-ethoxy)-[3,3']bipyridinyl-6-ylamine; 6'-amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-1-[2-(1-methyl-pyrrolidin-2-yl)-ethyl]-1H-[3,3']bipyridinyl-6-one; (4-{6-amino-5-[1-(2,4,6-trimethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; (4-{6-amino-5-[1-(2-chloro-6-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(4-fluoro-phenyl)-pyridin-2-ylamine; 6'-amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-1H-[3,3']bipyridinyl-6-one; 5'-bromo-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(4-dimethylamino-phenyl)-pyridin-2-ylamine; 5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-2'-methoxy-[3,3']bipyridinyl-6-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(1H-indol-5-yl)-pyridin-2-ylamine; (4-{6-amino-5-[1-(2,6-dichloro-phenyl)-propoxy]-pyridin-3-yl}-phenyl)-(3,5-dimethyl-piperazin-1-yl)-methanone; [4-(6-amino-5-benzyloxy-pyridin-3-yl)-phenyl]-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 3-(2,6-dichloro-3-fluoro-benzyloxy)-5-thiazol-2-yl-pyridin-2-ylamine; (4-{6-amino-5-[1-(2-fluoro-6-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 3-(2,6-dichloro-3-fluoro-benzyloxy)-5-(1-methyl-1H-imidazol-2-yl)-pyridin-2-ylamine; {4-[6-amino-5-(2,4,6-trimethyl-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {4-[6-amino-5-(2,3,5,6-tetramethyl-benzyloxy)-pyridin-3-yl]-phenyl}-(4-

pyrrolidin-1-yl-piperidin-1-yl)-methanone; {4-[6-amino-5-(2,4,6-trifluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; (4-{6-amino-5-[1-(2-fluoro-6-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-N-methyl-nicotinamidine; 6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-N-(2-morpholin-4-yl-ethyl)-nicotinamidine; (4-{6-amino-5-[1-(2,4,5-trifluoro-phenyl)-propoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; (4-{6-amino-5-[1-(6-chloro-2-fluoro-3-methyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 3-(1-{2-amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxy}-ethyl)-benzoic acid; and pharmaceutically acceptable salts, hydrates and solvates thereof.

In another embodiment, the invention provides a compound selected from the group consisting of: 3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide; 3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide; 3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; 3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; 3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; N-[2-(4-acetyl-piperazin-1-yl)-ethyl]-3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-benzamide; (3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; (3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; (3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone; (3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone; 4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-benzoic acid; 4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide; (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone; 4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; 4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; 4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; N-[2-(4-acetyl-piperazin-1-yl)-ethyl]-4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-benzamide; 2-[4-(2-Hydroxy-acetyl)-piperazin-1-yl]-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 3-[5-amino-6-(3-fluoro-2-

trifluoromethyl-benzyloxy)-pyrazin-2-yl]-benzoic acid; {3-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 3-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-N-[2-[ethyl-(2-methoxy-ethyl)-amino]-ethyl]-benzamide; {3-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; 3-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide; N-[2-(4-acetyl-piperazin-1-yl)-ethyl]-3-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-benzamide; {4-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {4-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; {4-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-phenyl}-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (3-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (3-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 3-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; 3-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; 3-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; 3-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(3-morpholin-4-yl-propyl)-benzamide; (3-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-cyclopropylamino-piperidin-1-yl)-methanone; 3-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-((S)-2-hydroxy-3-morpholin-4-yl-propyl)-benzamide; 3-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-((R)-2-hydroxy-3-pyrrolidin-1-yl-propyl)-benzamide; (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 2-diethylamino-ethanesulfonic acid (4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid (4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-dimethylamino-ethanesulfonic acid (4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-((R)-3-Hydroxy-pyrrolidin-1-yl)-ethanesulfonic acid (4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy}-pyrazin-2-yl}-phenyl)-amide; 2-pyrrolidin-1-ylethanesulfonic acid (4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-benzoic acid; 4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-((R)-2-hydroxy-3-pyrrolidin-1-yl-propyl)-benzamide; (4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-cyclopropylamino-piperidin-1-yl)-methanone; 4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-((S)-2-hydroxy-3-pyrrolidin-1-yl-propyl)-benzamide; 4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-((R)-2-hydroxy-3-morpholin-4-yl-propyl)-benzamide; 4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; (4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; (4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (4-[5-

amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-benzoic acid; (4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; (4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; (4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((R)-3-aminopyrrolidin-1-yl)-methanone; (4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-3-aminopyrrolidin-1-yl)-methanone hydrogen chloride; 4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; 4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide; 3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-benzoic acid; 3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; 3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; (3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; (3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; N-[2-(4-acetyl-piperazin-1-yl)-ethyl]-4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-benzamide; N-[2-(4-acetyl-piperazin-1-yl)-ethyl]-3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-benzamide; (3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; 3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide; (3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone; (3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone hydrochloride salt; (3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; 1-(4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-3-(2-morpholin-4-yl-ethyl)-urea; (R)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 1-(4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy}-pyrazin-2-yl}-phenyl)-3-(2-pyrrolidin-1-yl-ethyl)-urea; 4-methyl-piperazine-1-carboxylic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 1-(4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-3-(2-hydroxy-ethyl)-urea; (S)-3-amino-pyrrolidine-1-carboxylic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 1-(4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-3-(1-methyl-piperidin-4-yl)-urea; 4-methyl-piperazine-1-carboxylic acid (4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 1-(4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-

phenyl)-3-(2-hydroxy-ethyl)-urea; (S)-3-amino-pyrrolidine-1-carboxylic acid (4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 1-(4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-3-(1-methyl-piperidin-4-yl)-urea; 5-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophene-2-carboxylic acid; {5-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophen-2-yl}-(4-methyl-piperazin-1-yl)-methanone; {5-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophen-2-yl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {5-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophen-2-yl}-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; {5-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophen-2-yl}-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; 5-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophene-2-carboxylic acid (2-morpholin-4-yl-ethyl)-amide; 3-[1-(2,6-dichloro-3-fluorophenyl)ethoxy]-5-{5-[(4-methylpiperazin-1-yl)carbonyl]pyridin-2-yl}pyrazin-2-amine trifluoroacetate; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-pyridin-4-yl-pyrazin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(1H-pyrrol-2-yl)-pyrazin-2-ylamine; (6-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-pyridin-3-yl)-(4-methyl-piperazin-1-yl)-methanone; (2-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-pyridin-4-yl)-(4-methyl-piperazin-1-yl)-methanone; (6-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-pyridin-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (5-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-pyridin-3-yl)-(4-methyl-piperazin-1-yl)-methanone; (4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-pyridin-2-yl)-(4-methyl-piperazin-1-yl)-methanone; 6-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-morpholin-4-yl-ethyl)-nicotinamide; 5-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-morpholin-4-yl-ethyl)-nicotinamide; 6-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(3-morpholin-4-yl-propyl)-nicotinamide; 5-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(3-morpholin-4-yl-propyl)-nicotinamide; (6-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-pyridin-3-yl)-(4-isopropyl-piperazin-1-yl)-methanone; and pharmaceutically acceptable salts, hydrates and solvates thereof.

In another aspect, the invention provides a compound selected from the group consisting of the compounds shown in Table 1 and pharmaceutically acceptable salts, hydrates and solvates thereof.

In another aspect, the invention provides a compound selected from the group consisting of the compounds shown in Table 2 and pharmaceutically acceptable salts, hydrates and solvates thereof.

In another aspect, the invention provides a compound selected from the group consisting of the compounds shown in Table 3 and pharmaceutically acceptable salts, hydrates and solvates thereof.

In another aspect, the invention provides a compound selected from the group consisting of the compounds shown in Table 4 and pharmaceutically acceptable salts, hydrates and solvates thereof.

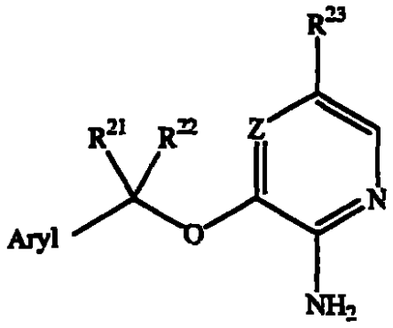
In another aspect, the invention provides a compound selected from the group consisting of the compounds shown in Table 5 and pharmaceutically acceptable salts, hydrates and solvates thereof.

In another aspect, the invention provides a compound selected from the group consisting of the compounds shown in Table 6 and pharmaceutically acceptable salts, hydrates and solvates thereof.

In another aspect, the invention provides a compound selected from the group consisting of the compounds shown in Table 7 and pharmaceutically acceptable salts, hydrates and solvates thereof.

In another aspect, the invention provides a compound selected from the group consisting of the compounds shown in Table 8 and pharmaceutically acceptable salts, hydrates and solvates thereof.

In another embodiment, the invention provides compounds having the following chemical structure (Formula 6):



(6)

wherein,

Z is CH or N;

Aryl is an optionally fused aryl or an optionally fused heteroaryl group which is optionally substituted by one or more substituents selected from the group consisting of a halogen, $-OR^{24}$, $-COR^{24}$, $-COOR^{24}$, $-CONR^{24}R^{25}$, -CN, $-NO_2$, $-S(O)_mR^{24}$, $-SO_2NR^{24}R^{25}$, perfluoroalkyl, lower alkyl, cycloalkyl, heterocycle, alkenyl, alkynyl, aryl, $-NR^{24}R^{25}$, $-NR^{24}C(O)R^{25}$ and $-NR^{24}S(O)_pR^{25}$;

R^{21} and R^{22} are independently selected from the group consisting of hydrogen, halogen, $-COR^{24}$, $-COOR^{24}$, $-CONR^{24}R^{25}$, -CN, perfluoroalkyl, lower alkyl, cycloalkyl, heterocycle, alkenyl, alkynyl, and aryl;

R^{22} is selected from the group consisting of:

an optionally fused aryl, heteroaryl, alicyclic or heterocyclic group, optionally substituted by one or more substituents selected from the group consisting of a halogen, $-(CH_2)_n-OR^{24}$, $-COR^{24}$, $-COOR^{24}$, $-CONR^{24}R^{25}$, -CN, $-NO_2$, $-S(O)_mR^{24}$, $-SO_2NR^{24}R^{25}$, perfluoroalkyl, -O-perfluoroalkyl, lower alkyl, cycloalkyl, heterocycle, heteroaryl, alkenyl, alkynyl, aryl, $-(CH_2)_n-NR^{24}R^{25}$, $-NR^{24}C(O)R^{25}$ and $-NR^{24}S(O)_pR^{25}$, wherein said heterocycle, heteroaryl and aryl substituents may be optionally substituted by a group selected from the group consisting of lower alkyl, halogen, $-C(O)NR^{24}R^{25}$, $NR^{24}R^{25}$, $NR^{24}C(O)R^{25}$ and $NR^{24}S(O)_pR^{25}$;

$-OR^{24}$, $-COR^{24}$, $-COOR^{24}$, -CN, $-NO_2$, $-S(O)_mR^{24}$, $-SO_2NR^{24}R^{25}$, perfluoroalkyl, cycloalkyl, heterocycle, alkenyl, and alkynyl;

R^{24} and R^{25} are independently selected from the group consisting of hydrogen, lower alkyl, cycloalkyl, alkenyl, alkynyl, aryl, aminoalkyl, alkylaminoalkyl, alkylaminocycloalkyl, dialkylaminoalkyl and $-(CH_2)_n$-heterocycle, wherein said $-(CH_2)_n$-heterocycle may be further substituted by one or more of lower alkyl, $-(CH_2)_n$-hydroxy, heterocycle and $-C(O)R^{26}$,

or R^{24} and R^{25} can combine to form a 5- to 6-membered heterocyclic ring having one or more heteroatoms selected from the group consisting of N, O, S, S(O) and SO_2, said 5- to 6-membered

33

heterocyclic ring may be optionally substituted by lower alkyl, $-(CH_2)_n$-heterocycle, cycloalkyl, halo, $-(CH_2)_n-NR^{25}R^{27}$, amino, $-C(O)R^{26}$, $-NR^{25}-C(O)OR^{27}$ and $-NR^{25}-C(O)R^{27}$;

wherein R^{26} and R^{27} are independently selected from the group consisting of hydrogen, lower alkyl, $-(CH_2)_n$-cycloalkyl and $-C(O)-(CH_2)_n-OH$;

except that when Z is N and R^{21} and R^{22} are H and Aryl is m-chlorophenyl, R^{23} is not piperazine;

m is 0, 1 or 2;

n is 0, 1, 2 or 3;

p is 1 or 2;

or a pharmaceutically acceptable salt thereof.

In preferred aspect of this embodiment, in the compound of Formula (6), R^{23} is aryl or heteroaryl.

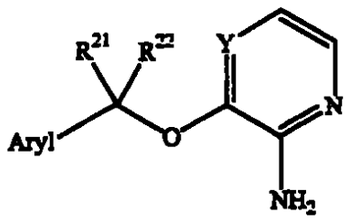
In another preferred aspect of this embodiment, when Z is N, R^{23} is not heteroalicyclic.

In another embodiment, the invention provides a pharmaceutical composition comprising any of the inventive compounds described herein. In particular aspects of this embodiment, the pharmaceutical composition comprises a compound of formula 1, a compound of formula 2, a compound of formula 3, a compound of formula 4, a compound of formula 5, a compound of formula 6, or a pharmaceutically acceptable salt, hydrate or solvate thereof, including particular aspects thereof as described above. In other particular aspects of this embodiment, the pharmaceutical composition comprises a compound selected from the compounds shown in Table 1, a compound selected from the compounds shown in Table 2, a compound selected from the compounds shown in Table 3, a compound selected from the compounds shown in Table 4, a compound selected from the compounds shown in Table 5, a compound selected from the compounds shown in Table 6, a compound selected from the compounds shown in Table 7, a compound selected from the compounds shown in Table 8, or a pharmaceutically acceptable salt, hydrate or solvate thereof.

Preferred compounds of the invention include those having c-MET inhibitory activity as defined by any one or more of IC_{50}, Ki, or percent inhibition. One skilled in the art can readily determine if a compound has such activity by carrying out the appropriate assay. In one embodiment, particularly preferred compounds have a c-MET IC_{50} of less than 5 μM, or less than 2 μM, or less than 1 μM, or less than 500 nM, or less than 400 nM, or less than 300 nM, or less than 200 nM, or less than 100 nM, or less than 50 nM. In another embodiment, particularly preferred compounds have a c-MET Ki of less than 5 μM or less than 2 μM, or less than 1 μM, or less than 500 nM, or less than 400 nM, or less than 300 nM, or less than 200 nM, or less than 100 nM, or less than 50 nM. In another embodiment, particularly preferred compounds have a c-MET inhibition at 1 μM of at least 10% or at least 20% or at least 30% or at least 40% or at least 50% or at least 60% or at least 70% or at least 80% or at least 90%.

In another embodiment, the invention provides a process of preparing the compound of Formula (6), comprising

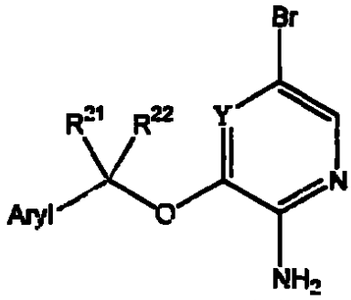
(i) brominating a compound of the formula (a):



(a)

to give a compound of formula (b):

and



(b)

ii. reacting (b) with a boronic acid or ester derivative of the formula $R^{23}B(OR)_2$ in the presence of a palladium catalyst;

wherein R is hydrogen or an alcohol protecting group and Aryl, R^{21}, R^{22}, and R^{23} are as defined defined above.

In another embodiment, R^{23} is aryl or heteroaryl.

In another embodiment the invention provides a method of treating a subject suffering from a condition for which inhibition of Met receptor tyrosine kinase is indicated, comprising administering to the subject a therapeutically effective amount of any of the inventive compounds described herein.

The chemical formulae referred to herein may exhibit the phenomena of tautomerism and structural isomerism. This invention encompasses any tautomeric or structural isomeric form and mixtures thereof which possess the ability to modulate RTK, CTK and/or STK activity and is not limited to any one tautomeric or structural isomeric form.

In addition, the formulae referred to herein may also exhibit stereoisomerism, in which such compounds may adopt an R or S configuration at chiral centers. Thus, this invention also encompasses any stereoisomeric form, their corresponding enantiomers (d- and l- or (+) and (-) isomers) and diastereomers thereof, and mixtures thereof, which possess the ability to modulate RTK, CTK and/or STK activity and is not limited to any one stereoisomeric form.

In particular embodiments, the compound is chosen from the compounds in Tables 1-8.

Another embodiment of the invention relates to a method of treating a subject suffering from a condition for which inhibition of protein kinase is indicated, comprising administering to the subject a therapeutically effective amount of any of the inventive compounds described herein.

Another aspect of this invention relates to a method for the modulation of the catalytic activity of a PK by contacting a PK with a compound of this invention or a physiologically acceptable salt thereof.

A further aspect of this invention is that the modulation of the catalytic activity of PKs using a compound of this invention may be carried out *in vitro* or *in vivo*.

A still further aspect of this invention is that the protein kinase whose catalytic activity is being modulated by a compound of this invention is selected from the group consisting of receptor protein tyrosine kinases, cellular tyrosine kinases and serine-threonine kinases.

It is an aspect of this invention that the receptor tyrosine protein kinase whose catalytic activity is modulated by a compound of this invention is selected from the group consisting of EGF, HER2, HER3, HER4, IR, IGF-1R, IRR, PDGFRα, PDGFRβ, CSFIR, C-Kit, C-fms, Flk-1R, Flk4, KDR/Flk-1, Flt-1, FGFR-1R, FGFR-2R, FGFR-3R, FGFR-4R, MET, DDR-1 and DDR-2.

In addition, it is an aspect of this invention that the cellular tyrosine kinase whose catalytic activity is modulated by a compound of this invention is selected from the group consisting of Src, Frk, Btk, Csk, Abl, ZAP70, Fes/Fps, Fak, Jak, Ack, Yes, Fyn, Lyn, Lck, Blk, Hck, Fgr and Yrk.

Another aspect of this invention is that the serine-threonine protein kinase whose catalytic activity is modulated by a compound of this invention is selected from the group consisting of CDK2, Raf, NEK and BUB1.

Another aspect of this invention relates to a method for treating or preventing a protein kinase related disorder in an organism comprising administering a therapeutically effective amount of any of the inventive compounds described herein to an organism, such as a mammal, particularly a human.

It is an aspect of this invention that the above-referenced protein kinase related disorder is selected from the group consisting of a receptor protein tyrosine kinase related disorder, a cellular tyrosine kinase disorder and a serine-threonine kinase related disorder.

In yet another aspect of this invention, the above referenced protein kinase related disorder is selected from the group consisting of a Met related disorder, an AUR2 related disorder, a ZC1 related disorder, a PDGFR related disorder, an IGFR related disorder and a flk related disorder.

The above referenced protein kinase related disorders include by way of example and not limitation, cancers such as lung cancer, NSCLC (non small cell lung cancer), bone cancer, pancreatic cancer, skin cancer, cancer of the head and neck, cutaneous or intraocular melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, colon cancer, breast cancer, gynecologic tumors (e.g., uterine sarcomas, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina or carcinoma of the vulva), Hodgkin's Disease, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system (e.g., cancer of the thyroid, parathyroid or adrenal glands), sarcomas of soft tissues, cancer of the urethra, cancer of the penis, prostate cancer, chronic or acute leukemia, solid tumors of childhood, lymphocytic lymphomas, cancer of the bladder, cancer of the kidney or ureter (e.g., renal cell carcinoma, carcinoma of the renal pelvis), pediatric malignancy, neoplasms of the central nervous system (e.g., primary CNS lymphoma, spinal axis tumors, brain stem glioma or pituitary adenomas), cancers of the bloodsuch as acute myeloid leukemia, chronic mueloid leukemia, etc, Barrett's esophagus (pre-malignant syndrome),

neoplastic cutaneous disease, psoriasis, mycoses fungoides and benign prostatic hypertrophy, diabetes related diseases such as diabetic retinopathy, retinal ischemia and retinal neovascularization, hepatic cirrhosis, cardiovascular disease such as atherosclerosis, immunological disease such as autoimmune disease and renal disease. Preferably, the disease is cancer such as acute myeloid leukemia and colorectal cancer.

The above referenced protein kinase related disorder also includes disorders selected from the group consisting of diabetes, a hyper-proliferation disorder, hyperproliferative disorders of the kidney, von Hippel-Lindau disease, restenosis, fibrosis, psoriasis, osteoarthritis, rheumatoid arthritis, an inflammatory disorder and angiogenesis in yet another aspect of this invention.

Additional disorders which may be treated or prevented using the compounds of this invention are immunological disorders such as autoimmune diseases (*e.g.*, AIDS, lupus, *etc.*) and cardiovascular disorders such as atherosclerosis.

It is an aspect of this invention that the protein kinase related disorder being treated or prevented by administration of a compound of this invention is a met kinase related disorder.

The organism in which the protein kinase related disorder is being treated or prevented is a human being in yet another aspect of this invention.

It is also an aspect of this invention that a compound described herein, or its salt, might be combined with other chemotherapeutic agents for the treatment of the diseases and disorders discussed above. For instance, a compound or salt of this invention might be combined with alkylating agents such as fluorouracil (5-FU) alone or in further combination with leukovorin; or other alkylating agents such as, without limitation, other pyrimidine analogs such as UFT, capecitabine, gemcitabine and cytarabine, the alkyl sulfonates, *e.g.*, busulfan (used in the treatment of chronic granulocytic leukemia), improsulfan and piposulfan; aziridines, *e.g.*, benzodepa, carboquone, meturedepa and uredepa; ethyleneimines and methylmelamines, *e.g.*, altretamine, triethylenemelamine, triethylenephosphoramide, triethylenethiophosphoramide and trimethylolmelamine; and the nitrogen mustards, *e.g.*, chlorambucil (used in the treatment of chronic lymphocytic leukemia, primary macroglobulinemia and non-Hodgkin's lymphoma), cyclophosphamide (used in the treatment of Hodgkin's disease, multiple myeloma, neuroblastoma, breast cancer, ovarian cancer, lung cancer, Wilm's tumor and rhabdomyosarcoma), estramustine, ifosfamide, novembrichin, prednimustine and uracil mustard (used in the treatment of primary thrombocytosis, non-Hodgkin's lymphoma, Hodgkin's disease and ovarian cancer); and triazines, *e.g.*, dacarbazine (used in the treatment of soft tissue sarcoma).

Likewise a compound or salt of this invention might be expected to have a beneficial effect in combination with other antimetabolite chemotherapeutic agents such as, without limitation, folic acid analogs, *e.g.* methotrexate (used in the treatment of acute lymphocytic leukemia, choriocarcinoma, mycosis fungiodes breast cancer, head and neck cancer and osteogenic sarcoma) and pteropterin; and the purine analogs such as mercaptopurine and thioguanine which find use in the treatment of acute granulocytic, acute lymphocytic and chronic granulocytic leukemias.

A compound or salt of this invention might also be expected to prove efficacious in combination with natural product based chemotherapeutic agents such as, without limitation, the vinca alkaloids, *e.g.*, vinblastin (used in the treatment of breast and testicular cancer), vincristine and vindesine; the epipodophyllotoxins, *e.g.*, etoposide and teniposide, both of which are useful in the treatment of testicular cancer and Kaposi's sarcoma; the antibiotic chemotherapeutic agents, *e.g.*, daunorubicin, doxorubicin, epirubicin, mitomycin (used to treat stomach, cervix, colon, breast, bladder and pancreatic cancer), dactinomycin, temozolomide, plicamycin, bleomycin (used in the treatment of skin, esophagus and genitourinary tract cancer); and the enzymatic chemotherapeutic agents such as L-asparaginase.

In addition to the above, a compound or salt of this invention might be expected to have a beneficial effect used in combination with the platinum coordination complexes (cisplatin, etc.); substituted ureas such as hydroxyurea; methylhydrazine derivatives, *e.g.*, procarbazine; adrenocortical suppressants, *e.g.*, mitotane, aminoglutethimide; and hormone and hormone antagonists such as the adrenocorticosteriods (*e.g.*, prednisone), progestins (*e.g.*, hydroxyprogesterone caproate); estrogens (*e.g.*, diethylstilbesterol); antiestrogens such as tamoxifen; androgens, *e.g.*, testosterone propionate; and aromatase inhibitors (such as anastrozole.

Finally, the combination of a compound of this invention might be expected to be particularly effective in combination with mitoxantrone or paclitaxel for the treatment of solid tumor cancers or leukemias such as, without limitation, acute myelogenous (non-lymphocytic) leukemia.

The above method can be carried out in combination with a chemotherapeutic agent selected from the group consisting of mitotic inhibitors, alkylating agents, antimetabolites, cell cycle inhibitors, enzymes, topoisomerase inhibitors, biological response modifiers, anti-hormones, antiangiogenic agents such as MMP-2, MMP-9 and COX-2 inhibitors, and anti-androgens.

Examples of useful COX-II inhibitors include VIOXX™, CELEBREX™ (alecoxib), valdecoxib, paracoxib, rofecoxib, and Cox 189. Examples of useful matrix metalloproteinase inhibitors are described in WO 96/33172 (published Oct. 24, 1996), WO 96/27583 (published Mar. 7, 1996), European Patent Application No. 97304971.1 (filed Jul. 8, 1997), European Patent Application No. 99308617.2 (filed Oct. 29, 1999), WO 98/07697 (published Feb. 26, 1998), WO 98/03516 (published Jan. 29, 1998), WO 98/34918 (published Aug. 13, 1998), WO 98/34915 (published Aug. 13, 1998), WO 98/33768 (published Aug. 6, 1998), WO 98/30566 (published Jul. 16, 1998), European Patent Publication 606,046 (published Jul. 13, 1994), European Patent Publication 931,788 (published Jul. 28, 1999), WO 90/05719 (published May 31, 1990), WO 99/52910 (published Oct. 21, 1999), WO 99/52889 (published Oct. 21, 1999), WO 99/29667 (published Jun. 17, 1999), PCT International Application No. PCT/IB98/01113 (filed Jul. 21, 1998), European Patent Application No. 99302232.1 (filed Mar. 25, 1999), Great Britain patent application number 9912961.1 (filed Jun. 3, 1999), U.S. Provisional Application No. 60/148,464 (filed Aug. 12, 1999), U.S. Pat. No. 5,863,949 (issued Jan. 26, 1999), U.S. Pat. No. 5,861,510 (issued Jan. 19, 1999), and European Patent Publication 780,386 (published Jun. 25, 1997), all of which are incorporated herein in their entireties by reference. Preferred MMP-2 and MMP-9 inhibitors are those that have little or no activity inhibiting MMP-1. More preferred, are those that selectively inhibit MMP-2

and/or MMP-9 relative to the other matrix-metalloproteinases (i.e. MMP-1, MMP-3, MMP-4, MMP-5, MMP-6, MMP-7, MMP-8, MMP-10, MMP-11, MMP-12, and MMP-13).

Some specific examples of MMP inhibitors useful in the present invention are AG-3340, RO 32-3555, RS 13-0830, and the compounds recited in the following list:

3-[[4-(4-fluoro-phenoxy)-benzenesulfonyl]-(1-hydroxycarbamoyl-cyclopentyl)- amino]-propionic acid; 3-exo-3-[4-(4-fluoro-phenoxy)-benzenesulfonylamino]-8-oxa-bicyclo[3.2. 1]octane-3-carboxylic acid hydroxyamide; (2R, 3R) 1-[4-(2-chloro-4-fluoro-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide; 4-[4-(4-fluoro-phenoxy)-benzenesulfonylamino]-tetrahydro-pyran-4-carboxylic acid hydroxyamide; 3-[[4-(4-fluoro-phenoxy)-benzenesulfonyl]-(1-hydroxycarbamoyl-cyclobutyl)-amino]-propionic acid; 4-[4-(4-chloro-phenoxy)-benzenesulfonylamino]-tetrahydro-pyran-4-carboxylic acid hydroxyamide; (R) 3-[4-(4-chloro-phenoxy)-benzenesulfonylamino]-tetrahydro-pyran-3-carboxylic acid hydroxyamide; (2R, 3R) 1-[4-(4-fluoro-2-methyl-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide; 3-[[(4-(4-fluoro-phenoxy)-benzenesulfonyl]-(1-hydroxycarbamoyl-1-methyl-ethyl)-amino]-propionic acid; 3-[[4-(4-fluoro-phenoxy)-benzenesulfonyl]-(4-hydroxycarbamoyl-tetrahydro-pyran-4-yl)-amino]-propionic acid; 3-exo-3-[4-(4-chloro-phenoxy)-benzenesulfonylamino]-8-oxa-bicyclo[3.2. 1]octane-3-carboxylic acid hydroxyamide; 3-endo-3-[4-(4-fluoro-phenoxy)-benzenesulfonylamino]-8-oxa-bicyclo[3.2. 1]octane-3-carboxylic acid hydroxyamide; and (R) 3-[4-(4-fluoro-phenoxy)-benzenesulfonylamino]-tetrahydro-furan-3-carboxylic acid hydroxyamide; and pharmaceutically acceptable salts and solvates of said compounds.

Other anti-angiogenesis agents, including other COX-II inhibitors and other MMP inhibitors, can also be used in the present invention.

A compound of the invention can also be used with signal transduction inhibitors, such as agents that can inhibit EGFR (epidermal growth factor receptor) responses, such as EGFR antibodies, EGF antibodies, and molecules that are EGFR inhibitors; VEGF (vascular endothelial growth factor) inhibitors; and erbB2 receptor inhibitors, such as organic molecules or antibodies that bind to the erbB2 receptor, for example, HERCEPTIN® (Genentech, Inc. of South San Francisco, Calif., USA). EGFR inhibitors are described in, for example in WO 95/19970 (published Jul. 27, 1995), WO 98/14451 (published Apr. 9, 1998), WO 98/02434 (published Jan. 22, 1998), and U.S. Pat. No. 5,747,498 (issued May 5, 1998), and such substances can be used in the present invention as described herein.

EGFR-inhibiting agents include, but are not limited to, the monoclonal antibodies C225 and anti-EGFR 22Mab (ImClone Systems Incorporated of New York, N.Y., USA), the compounds ZD-1839 (AstraZeneca), BIBX-1382 (Boehringer Ingelheim), MDX-447 (Medarex Inc. of Annandale, N.J., USA), and OLX-103 (Merck & Co. of Whitehouse Station, N.J., USA), VRCTC-310 (Ventech Research) and EGF fusion toxin (Seragen Inc. of Hopkinton, Mass.).

These and other EGFR-inhibiting agents can be used in the present invention.

VEGF inhibitors, for example 3-(2,4-Dimethylpyrrol-5-yl)methylene-2-indolinone, 5-(5-Fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylamino-ethyl)-amide, 3-[2,4-dimethyl-5-oxo-1,2-dihydroindole-3-ylidenemethyl)-1H-pyrrol-3-yl-propionic acid (Sugen Inc. of South San Francisco, Calif., USA), can also be combined with an inventive compound described

36

herein. VEGF inhibitors are described in, for example in WO 99/24440, PCT International Application PCT/IB99/00797 (filed May 3, 1999), in WO 95/21613, WO 99/61422 (published Dec. 2,1999), U.S. Pat. No. 5,834,504 (issued Nov. 10, 1998), WO 01/60814,WO 02/04407, WO 98/50356, U.S. Pat. No. 5,883,113 (issued Mar. 16, 1999), U.S. Pat. No. 5,886,020 (issued Mar. 23, 1999), U.S. Pat. No. 5,792,783 (issued Aug. 11, 1998), WO 99/10349 (published Mar. 4, 1999), WO 97/32856 (published Sep. 12, 1997), WO 97/22596 (published Jun.26, 1997), WO 98/54093 (published Dec. 3, 1998), WO 98/02438 (published Jan. 22, 1998), WO 99/16755 (published Apr. 8, 1999), and WO 98/02437 (published Jan. 22, 1998), all of which are incorporated herein in their entireties by reference. Other examples of some specific VEGF inhibitors useful in the present invention are IM862 (Cytran Inc. of Kirkland, Wash., USA); anti-VEGF monoclonal antibody of Genentech, Inc. of South San Francisco, Calif.; and angiozyme, a synthetic ribozyme from Ribozyme (Boulder, Colo.) and Chiron (Emeryville, Calif.). These and other VEGF inhibitors can be used in the present invention as described herein.

ErbB2 receptor inhibitors, such as GW-282974 (Glaxo Wellcome plc), and the monoclonal antibodies AR-209 (Aronex Pharmaceuticals Inc. of TheWoodlands, Tex., USA) and 2B-1 (Chiron), can furthermore be combined with a compound any of the inventive compounds described herein, for example those indicated in WO 98/02434 (published Jan. 22, 1998), WO 99/35146 (published Jul. 15, 1999), WO 99/35132 (published Jul. 15, 1999), WO 98/02437 (published Jan. 22, 1998), WO 97/13760 (published Apr. 17, 1997), WO 95/19970 (published Jul. 27, 1995), U.S. Pat. No. 5,587,458 (issued Dec. 24, 1996), and U.S. Pat. No. 5,877,305 (issued Mar. 2, 1999), which are all hereby incorporated herein in their entireties by reference. ErbB2 receptor inhibitors useful in the present invention are also described in U.S. Provisional Application No. 60/117,341, filed Jan. 27, 1999, and in U.S. Provisional Application No. 60/117,346, filed Jan. 27,1999, both of which are incorporated in their entireties herein by reference. The erbB2 receptor inhibitor compounds and substance described in the aforementioned PCT applications, U.S. patents, and U.S. provisional applications, as well as other compounds and substances that inhibit the erbB2 receptor, can be used with the inventive compounds described herein.

The inventive compounds described herein can also be used with other agents useful in treating cancer, including, but not limited to, agents capable of enhancing antitumor immune responses, such as CTLA4 (cytotoxic lymphocite antigen 4) antibodies, and other agents capable of blocking CTLA4; and anti-proliferative agents such as other farnesyl protein transferase inhibitors, for example the farnesyl protein transferase inhibitors described in the references cited in the "Background" section, of US Patent No. 6,258,824 B1. Specific CTLA4 antibodies that can be used in the present invention include those described in U.S. Provisional Application 60/113,647 (filed Dec. 23, 1998) which is incorporated by reference in its entirety, however other CTLA4 antibodies can be used in the present invention.

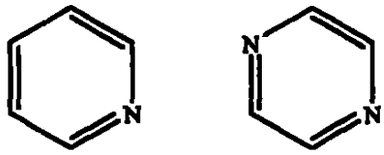
The above method can be also be carried out in combination with radiation therapy, wherein the amount of the inventive compound in combination with the radiation therapy is effective in treating the above diseases. Techniques for administering radiation therapy are known in the art, and these techniques can be used in the combination therapy described herein. The administration of the compound of the invention in this combination therapy can be determined as described herein.

Another aspect of the invention is directed to the use of any of the inventive compounds described herein in the preparation of a medicament, which is useful in the treatment of a disease mediated by abnormal Met kinase activity, such as cancer.

DETAILED DESCRIPTION

Definitions

The terms pyridine and pyrazine refer to the following structures respectively:



"Pharmaceutically acceptable salt" or "pharmaceutically acceptable salt thereof" refer to those salts which retain the biological effectiveness and properties of the free bases and which are obtained by reaction with inorganic or organic acids, such as hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, nitric acid, phosphoric acid, methanesulfonic acid, ethanesulfonic acid, *p*-toluenesulfonic acid, salicylic acid, acetic acid, benzenesulfonic acid (besylate), benzoic acid, camphorsulfonic acid, citric acid, fumaric acid, gluconic acid, glutamic acid, isethionic acid, lactic acid, maleic acid, malic acid, mandelic acid, mucic acid, pamoic acid, pantothenic acid, succinic acid, tarteric acid, and the like.

A "pharmaceutical composition" refers to a mixture of one or more of the compounds described herein, or physiologically acceptable salts thereof, with other chemical components, such as physiologically acceptable carriers and excipients. The purpose of a pharmaceutical composition is to facilitate administration of a compound to an organism.

As used herein, a "physiologically acceptable carrier" refers to a carrier or diluent that does not cause significant irritation to an organism and does not abrogate the biological activity and properties of the administered compound.

An "excipient" refers to an inert substance added to a pharmaceutical composition to further facilitate administration of a compound. Examples, without limitation, of excipients include calcium carbonate, calcium phosphate, various sugars and types of starch, cellulose derivatives (including microcrystalline cellulose), gelatin, vegetable oils, polyethylene glycols, diluents, granulating agents, lubricants, binders, disintegrating agents, and the like.

Compounds that have the same molecular formula but differ in the nature or sequence of bonding of their atoms or arrangements of their atoms in space are termed "isomers." Isomers that differ in the arrangement of their atoms in space are termed "stereoisomers". Stereoisomers that are not mirror images of one another are termed "diastereomers" and those that are non-superimposable mirror images of each other are termed "enantiomers". When a compound has an asymmetric center, for example, it is bonded to four different groups, a pair of enantiomers is possible. An enantiomer can be characterized by the absolute configuration of its asymmetric center and is described by the R- and S-sequencing rules of Cahn and Prelog, or by the manner in which the molecule rotates the plane of polarized light and designated as dextrorotatory or levorotatory (i.e., as (+) or (-)-isomers respectively).

37

A chiral compound can exist as either individual enantiomer or as a mixture thereof. A mixture containing equal proportions of the enantiomers is called a "racemic mixture".

The compounds of this invention may possess one or more asymmetric centers; such compounds can therefore be produced as individual (R)- or (S)- stereoisomers or as mixtures thereof. Unless indicated otherwise, the description or naming of a particular compound in the specification and claims is intended to include both individual enantiomers and mixtures, racemic or otherwise, thereof. The methods for the determination of stereochemistry and the separation of stereoisomers are well-known in the art (see discussion in Chapter 4 of "Advanced Organic Chemistry", 4th edition J. March, John Wiley and Sons, New York, 1992).

The inventive compounds herein may exhibit the phenomena of tautomerism and structural isomerism. This invention encompasses any tautomeric or structural isomeric form and mixtures thereof which possess the ability to modulate RTK, CTK and/or STK activity and is not limited to any one tautomeric or structural isomeric form.

It is contemplated that an inventive compound as described herein would be metabolized by enzymes in the body of the organism such as human being to generate a metabolite that can modulate the activity of the protein kinases. Such metabolites are within the scope of the present invention.

As used herein, "PK" refers to receptor protein tyrosine kinase (RTKs), non-receptor or "cellular" tyrosine kinase (CTKs) and serine-threonine kinase (STKs).

The term "method" refers to manners, means, techniques and procedures for accomplishing a given task including, but not limited to, those manners, means, techniques and procedures either known to, or readily developed from known manners, means, techniques and procedures by, practitioners of the chemical, pharmaceutical, biological, biochemical and medical arts.

As used herein, the term "modulation" or "modulating" refers to the alteration of the catalytic activity of RTKs, CTKs and STKs. In particular, modulating refers to the activation of the catalytic activity of RTKs, CTKs and STKs, preferably the activation or inhibition of the catalytic activity of RTKs, CTKs and STKs, depending on the concentration of the compound or salt to which the RTK, CTK or STK is exposed or, more preferably, the inhibition of the catalytic activity of RTKs, CTKs and STKs.

The term "catalytic activity" as used herein refers to the rate of phosphorylation of tyrosine under the influence, direct or indirect, of RTKs and/or CTKs or the phosphorylation of serine and threonine under the influence, direct or indirect, of STKs.

The term "contacting" as used herein refers to bringing a compound of this invention and a target PK together in such a manner that the compound can affect the catalytic activity of the PK, either directly, *i.e.*, by interacting with the kinase itself, or indirectly, *i.e.*, by interacting with another molecule on which the catalytic activity of the kinase is dependent. Such "contacting" can be accomplished *in vitro*, *i.e.*, in a test tube, a petri dish or the like. In a test tube, contacting may involve only a compound and a PK of interest or it may involve whole cells. Cells may also be maintained or grown in cell culture dishes and contacted with a compound in that environment. In this context, the ability of a particular compound to affect a PK related disorder, *i.e.*, the IC_{50} of the compound, defined below, can be determined before use of the compounds *in vivo* with more complex living organisms is attempted. For

cells outside the organism, multiple methods exist, and are well-known to those skilled in the art, to get the PKs in contact with the compounds including, but not limited to, direct cell microinjection and numerous transmembrane carrier techniques.

"*In vitro*" refers to procedures performed in an artificial environment such as, *e.g.*, without limitation, in a test tube or culture medium. The skilled artisan will understand that, for example, an isolated PK may be contacted with a modulator in an *in vitro* environment. Alternatively, an isolated cell may be contacted with a modulator in an *in vitro* environment.

As used herein, "*In vivo*" refers to procedures performed within a living organism such as, without limitation, a mouse, rat, rabbit, ungulate, bovine, equine, porcine, canine, feline, primate, or human.

As used herein, "PK related disorder," "PK driven disorder," and "abnormal PK activity" all refer to a condition characterized by inappropriate, *i.e.*, under or, more commonly, over, PK catalytic activity, where the particular PK can be an RTK, a CTK or an STK. Inappropriate catalytic activity can arise as the result of either: (1) PK expression in cells which normally do not express PKs, (2) increased PK expression leading to unwanted cell proliferation, differentiation and/or growth, or, (3) decreased PK expression leading to unwanted reductions in cell proliferation, differentiation and/or growth. Over-activity of a PK refers to either amplification of the gene encoding a particular PK or production of a level of PK activity which can correlate with a cell proliferation, differentiation and/or growth disorder (that is, as the level of the PK increases, the severity of one or more of the symptoms of the cellular disorder increases). Under-activity is, of course, the converse, wherein the severity of one or more symptoms of a cellular disorder increases as the level of the PK activity decreases.

As used herein, the terms "prevent", "preventing" and "prevention" refer to a method for barring an organism from acquiring a PK related disorder in the first place.

As used herein, the terms "treat", "treating" and "treatment" refer to a method of alleviating or abrogating a PK mediated cellular disorder and/or its attendant symptoms. With regard particularly to cancer, these terms simply mean that the life expectancy of an individual affected with a cancer will be increased or that one or more of the symptoms of the disease will be reduced.

The term "organism" refers to any living entity comprised of at least one cell. A living organism can be as simple as, for example, a single eukaryotic cell or as complex as a mammal. In a preferred aspect, the organism is a mammal. In a particularly preferred aspect, the mammal is a human being.

The term "therapeutically effective amount" as used herein refers to that amount of the compound being administered which will relieve to some extent one or more of the symptoms of the disorder being treated. In reference to the treatment of cancer, a therapeutically effective amount refers to that amount which has the effect of (1) reducing the size of the tumor, (2) inhibiting (that is, slowing to some extent, preferably stopping) tumor metastasis, (3) inhibiting to some extent (that is, slowing to some extent, preferably stopping) tumor growth, and/or, (4) relieving to some extent (or, preferably, eliminating) one or more symptoms associated with the cancer.

By "monitoring" is meant observing or detecting the effect of contacting a compound with a cell expressing a particular PK. The observed or detected effect can be a change in cell phenotype, in the

38

catalytic activity of a PK or a change in the interaction of a PK with a natural binding partner. Techniques for observing or detecting such effects are well-known in the art. For example, the catalytic activity of a PK may be observed by determining the rate or amount of phosphorylation of a target molecule.

Reference to compounds of the invention includes pharmaceutically acceptable salts, solvates and hydrates thereof.

"Cell phenotype" refers to the outward appearance of a cell or tissue or the biological function of the cell or tissue. Examples, without limitation, of a cell phenotype are cell size, cell growth, cell proliferation, cell differentiation, cell survival, apoptosis, and nutrient uptake and use. Such phenotypic characteristics are measurable by techniques well-known in the art.

A "natural binding partner" refers to a polypeptide that binds to a particular PK in a cell. Natural binding partners can play a role in propagating a signal in a PK-mediated signal transduction process. A change in the interaction of the natural binding partner with the PK can manifest itself as an increased or decreased concentration of the PK/natural binding partner complex and, as a result, in an observable change in the ability of the PK to mediate signal transduction.

As used herein, "administer" or "administration" refers to the delivery of a compound or salt of the present invention or of a pharmaceutical composition containing a compound or salt of this invention to an organism for the purpose of prevention or treatment of a PK-related disorder.

A "pharmaceutical composition" refers to a mixture of one or more of the compounds described herein, or pharmaceutically acceptable salts or prodrugs thereof, with other chemical components, such as pharmaceutically acceptable excipients. The purpose of a pharmaceutical composition is to facilitate administration of a compound to an organism.

"Pharmaceutically acceptable excipient" refers to an inert substance added to a pharmaceutical composition to further facilitate administration of a compound. Examples, without limitation, of excipients include calcium carbonate, calcium phosphate, various sugars and types of starch, cellulose derivatives, gelatin, vegetable oils and polyethylene glycols.

"Pharmaceutically acceptable salt" refers to those salts which retain the biological effectiveness and properties of the parent compound. Such salts include:

(1) acid addition salt which is obtained by reaction of the free base of the parent compound with inorganic acids such as hydrochloric acid, hydrobromic acid, nitric acid, phosphoric acid, sulfuric acid, and perchloric acid and the like, or with organic acids such as acetic acid, oxalic acid, (D) or (L) malic acid, maleic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid, tartaric acid, citric acid, succinic acid or malonic acid and the like, preferably hydrochloric acid or (L)-malic acid; and

(2) salts formed when an acidic proton present in the parent compound either is replaced by a metal ion, e.g., an alkali metal ion, an alkaline earth ion, or an aluminum ion; or coordinates with an organic base such as ethanolamine, diethanolamine, triethanolamine, tromethamine, N-methylglucamine, and the like.

The inventive compounds described herein may also act as a prodrug. A "prodrug" refers to an agent, which is converted into the parent drug in vivo. Prodrugs are often useful because, in some situations, they may be easier to administer than the parent drug. They may, for instance, be bioavailable by oral administration whereas the parent drug is not. The prodrug may also have improved solubility in pharmaceutical compositions over the parent drug.

Indications

The PKs whose catalytic activity is modulated by the compounds of this invention include protein tyrosine kinases of which there are two types, receptor tyrosine kinases (RTKs) and cellular tyrosine kinases (CTKs), and serine-threonine kinases (STKs). RTK mediated signal transduction, is initiated by extracellular interaction with a specific growth factor (ligand), followed by receptor dimerization, transient stimulation of the intrinsic protein tyrosine kinase activity and phosphorylation. Binding sites are thereby created for intracellular signal transduction molecules and lead to the formation of complexes with a spectrum of cytoplasmic signaling molecules that facilitate the appropriate cellular response (*e.g.*, cell division, metabolic effects on the extracellular microenvironment, *etc.*). See, Schlessinger and Ullrich, *Neuron*, 9:303-391 (1992).

It has been shown that tyrosine phosphorylation sites on growth factor receptors function as high-affinity binding sites for SH2 (src homology) domains of signaling molecules. Fantl *et al.*, *Cell*, 69:413-423 (1992), Songyang *et al.*, *Mol. Cell. Biol.*, 14:2777-2785 (1994), Songyang *et al.*, *Cell*, 72:767-778 (1993), and Koch *et al.*, *Science*, 252:668-678 (1991). Several intracellular substrate proteins that associate with RTKs have been identified. They may be divided into two principal groups: (1) substrates that have a catalytic domain, and (2) substrates which lack such domain but which serve as adapters and associate with catalytically active molecules. Songyang *et al.*, *Cell*, 72:767-778 (1993). The specificity of the interactions between receptors and SH2 domains of their substrates is determined by the amino acid residues immediately surrounding the phosphorylated tyrosine residue. Differences in the binding affinities between SH2 domains and the amino acid sequences surrounding the phosphotyrosine residues on particular receptors are consistent with the observed differences in their substrate phosphorylation profiles. Songyang *et al.*, *Cell*, 72:767-778 (1993). These observations suggest that the function of each RTK is determined not only by its pattern of expression and ligand availability but also by the array of downstream signal transduction pathways that are activated by a particular receptor. Thus, phosphorylation provides an important regulatory step which determines the selectivity of signaling pathways recruited by specific growth factor receptors, as well as differentiation factor receptors.

STKs, being primarily cytosolic, affect the internal biochemistry of the cell, often as a down-line response to a PTK event. STKs have been implicated in the signaling process which initiates DNA synthesis and subsequent mitosis leading to cell proliferation.

Thus, PK signal transduction results in, among other responses, cell proliferation, differentiation, growth and metabolism. Abnormal cell proliferation may result in a wide array of disorders and diseases, including the development of neoplasia such as carcinoma, sarcoma, glioblastoma and

hemangioma, disorders such as leukemia, psoriasis, arteriosclerosis, arthritis and diabetic retinopathy and other disorders related to uncontrolled angiogenesis and/or vasculogenesis.

A precise understanding of the mechanism by which the compounds of the invention, in particular, the compounds generated *in vivo* from the compounds of the invention, inhibit PKs is not required in order to practice the present invention. However, while not hereby being bound to any particular mechanism or theory, it is believed that the compounds interact with the amino acids in the catalytic region of PKs. PKs typically possess a bi-lobate structure wherein ATP appears to bind in the cleft between the two lobes in a region where the amino acids are conserved among PKs. Inhibitors of PKs are believed to bind by non-covalent interactions such as hydrogen bonding, van der Waals forces and ionic interactions in the same general region where the aforesaid ATP binds to the PKs. More specifically, it is thought that the compounds of this invention binds in the general space normally occupied by the adenine ring of ATP.

In another aspect, the protein kinase, the catalytic activity of which is modulated by contact with a compound of this invention, is a protein tyrosine kinase, more particularly, a receptor protein tyrosine kinases. Among the receptor protein tyrosine kinases whose catalytic activity can be modulated with a compound of this invention, or salt thereof, are, without limitation, selected from the group consisting of Met, Flk, FGFR, PDGFR, HER, IR, IGF, IRR, CSFIR, C-Kit, C-fms, flt. In a preferred aspect, the receptor protein tyrosine kinase whose catalytic activity can be modulated with a compound of this invention, or salt thereof.

The protein tyrosine kinase whose catalytic activity is modulated by contact with a compound of this invention, or a salt thereof, can also be a non-receptor or cellular protein tyrosine kinase (CTK). Thus, the catalytic activity of CTKs such as, without limitation, Src, Frk, Btk, Csk, Abl, ZAP70, Fes, Fps, Fak, Jak, Ack, Yes, Fyn, Lyn, Lck, Blk, Hck, Fgr, Aur2 and Yrk may be modulated by contact with a compound or salt of this invention.

Still another group of PKs which may have their catalytic activity modulated by contact with a compound of this invention are the serine-threonine protein kinases such as, without limitation, CDK2, Raf, NEK (including NEK 4a, NEK 4b, NEK 5 and NEK 6) and BUB1.

In another aspect, this invention relates to a method for treating or preventing a PK related disorder by administering a therapeutically effective amount of a compound of this invention, or a salt thereof, to an organism.

It is also an aspect of this invention that a pharmaceutical composition containing a compound of this invention, or a salt thereof, is administered to an organism for the purpose of preventing or treating a PK related disorder.

This invention is therefore directed to compounds that modulate PK signal transduction by affecting the enzymatic activity of RTKs, CTKs and/or STKs, thereby interfering with the signals transduced by such proteins. More particularly, the present invention is directed to compounds which modulate RTK, CTK and/or STK mediated signal transduction pathways as a therapeutic approach to cure many kinds of solid tumors, including but not limited to carcinomas, sarcomas including Kaposi's sarcoma, erythroblastoma, glioblastoma, meningioma, astrocytoma, melanoma and myoblastoma.

cancers such as lung cancer, NSCLC (non small cell ling cancer), bone cancer, pancreatic cancer, skin cancer, cancer of the head and neck, cutaneous or intraocular melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, colon cancer, breast cancer, gynecologic tumors (e.g., uterine sarcomas, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina or carcinoma of the vulva), Hodgkin's Disease, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system (e.g., cancer of the thyroid, parathyroid or adrenal glands), sarcomas of soft tissues, cancer of the urethra, cancer of the penis, prostate cancer, chronic or acute leukemia, solid tumors of childhood, lymphocytic lymphomas, cancer of the bladder, cancer of the kidney or ureter (e.g., renal cell carcinoma, carcinoma of the renal pelvis), pediatric malignancy, neoplasms of the central nervous system (e.g., primary CNS lymphoma, spinal axis tumors, brain stem glioma or pituitary adenomas), cancers of the bloodsuch as acute myeloid leukemia, chronic mueloid leukemia, etc, Barrett's esophagus (pre-malignant syndrome), neoplastic cutaneous disease, psoriasis, mycoses fungoides and benign prostatic hypertrophy, diabetes related diseases such as diabetic retinopathy, retinal ischemia and retinal neovascularization, hepatic cirrhosis, cardiovascular disease such as atherosclerosis, immunological disease such as autoimmune disease and renal disease. Preferably, the disease is cancer such as acute myeloid leukemia and colorectal cancer.

Further examples, without limitation, of the types of disorders related to inappropriate PK activity that the compounds described herein may be useful in preventing, treating and studying, are cell proliferative disorders, fibrotic disorders, metabolic disorders and infectious diseases.

Cell proliferative disorders, which may be prevented, treated or further studied by the present invention include cancer, blood vessel proliferative disorders and mesangial cell proliferative disorders.

Blood vessel proliferative disorders refer to disorders related to abnormal vasculogenesis (blood vessel formation) and angiogenesis (spreading of blood vessels). While vasculogenesis and angiogenesis play important roles in a variety of normal physiological processes such as embryonic development, corpus luteum formation, wound healing and organ regeneration, they also play a pivotal role in cancer development where they result in the formation of new capillaries needed to keep a tumor alive. Other examples of blood vessel proliferation disorders include arthritis, where new capillary blood vessels invade the joint and destroy cartilage, and ocular diseases, like diabetic retinopathy, where new capillaries in the retina invade the vitreous, bleed and cause blindness.

Normal vasculogenesis and angiogenesis play important roles in a variety of physiological processes such as embryonic development, wound healing, organ regeneration and female reproductive processes such as follicle development in the corpus luteum during ovulation and placental growth after pregnancy. Folkman & Shing, *J. Biological Chem.*, 267(16):10931-10934 (1992). Uncontrolled vasculogenesis and/or angiogenesis has been associated with diseases such as diabetes as well as with malignant solid tumors that rely on vascularization for growth. Klagsburn & Soker, *Current Biology*, 3(10):699-702 (1993); Folkham, *J. Natl. Cancer Inst.*, 82:4-6 (1991); Weidner, *et al.*, *New Engl. J. Med.*, 324:1-5 (1991).

As presently understood, the role of VEGF in endothelial cell proliferation and migration during angiogenesis and vasculogenesis indicates an important role for the KDR/FLK-1 receptor in these processes. Diseases such as diabetes mellitus (Folkman, 198, in XIth Congress of Thrombosis and Haemostasis (Verstraete, *et al.*, eds.), pp. 583-596, Leuven University Press, Leuven) and arthritis, as well as malignant tumor growth may result from uncontrolled angiogenesis. See *e.g.*, Folkman, *N. Engl. J. Med.*, 285:1182-1186 (1971). The receptors to which VEGF specifically binds are an important and powerful therapeutic target for the regulation and modulation of vasculogenesis and/or angiogenesis and a variety of severe diseases which involve abnormal cellular growth caused by such processes. Plowman, *et al.*, *DN&P*, 7(6):334-339 (1994). More particularly, the KDR/FLK-1 receptor's highly specific role in neovascularization make it a choice target for therapeutic approaches to the treatment of cancer and other diseases which involve the uncontrolled formation of blood vessels.

Thus, one aspect of the present invention relates to compounds capable of regulating and/or modulating tyrosine kinase signal transduction including KDR/FLK-1 receptor signal transduction in order to inhibit or promote angiogenesis and/or vasculogenesis, that is, compounds that inhibit, prevent, or interfere with the signal transduced by KDR/FLK-1 when activated by ligands such as VEGF. Although it is believed that the compounds of the present invention act on a receptor or other component along the tyrosine kinase signal transduction pathway, they may also act directly on the tumor cells that result from uncontrolled angiogenesis.

Thus, in one aspect, this invention is directed to compounds that regulate, modulate and/or inhibit vasculogenesis and/or angiogenesis by affecting the enzymatic activity of the KDR/FLK-1 receptor and interfering with the signal transduced by KDR/FLK-1. In another aspect, the present invention is directed to compounds which regulate, modulate and/or inhibit the KDR/FLK-1 mediated signal transduction pathway as a therapeutic approach to the treatment of many kinds of solid tumors including, but not limited to, glioblastoma, melanoma and Kaposi's sarcoma, and ovarian, lung, mammary, prostate, pancreatic, colon and epidermoid carcinoma. In addition, data suggest the administration of compounds which inhibit the KDR/Flk-1 mediated signal transduction pathway may also be used in the treatment of hemangioma, restenosis and diabetic retinopathy.

A further aspect of this invention relates to the inhibition of vasculogenesis and angiogenesis by other receptor-mediated pathways, including the pathway comprising the flt-1 receptor.

Receptor tyrosine kinase mediated signal transduction is initiated by extracellular interaction with a specific growth factor (ligand), followed by receptor dimerization, transient stimulation of the intrinsic protein tyrosine kinase activity and autophosphorylation. Binding sites are thereby created for intracellular signal transduction molecules which leads to the formation of complexes with a spectrum of cytoplasmic signaling molecules that facilitate the appropriate cellular response, *e.g.*, cell division and metabolic effects to the extracellular microenvironment. See, Schlessinger and Ullrich, *Neuron*, 9:1-20 (1992).

The close homology of the intracellular regions of KDR/FLK-1 with that of the PDGF-β receptor (50.3% homology) and/or the related flt-1 receptor indicates the induction of overlapping signal transduction pathways. For example, for the PDGF-β receptor, members of the src family (Twamley *et*

al., *Proc. Natl. Acad. Sci. USA*, 90:7696-7700 (1993)), phosphatidylinositol-3'-kinase (Hu *et al.*, *Mol. Cell. Biol.*, 12:981-990 (1992), phospholipase cγ (Kashishian & Cooper, *Mol. Cell. Biol.*, 4:49-51 (1993)), ras-GTPase-activating protein, (Kashishian *et al.*, *EMBO J.*, 11:1373-1382 (1992), PTP-ID/syp (Kazlauskas *et al.*, *Proc. Natl. Acad. Sci. USA*, 90:6939-6943 (1993)), Grb2 (Arvidsson *et al.*, *Mol. Cell. Biol.*, 14:6715-6726 (1994)), and the adapter molecules Shc and Nck (Nishimura *et al.*, *Mol. Cell. Biol.*, 13:6889-6896 (1993)), have been shown to bind to regions involving different autophosphorylation sites. See generally, Claesson-Welsh, *Prog. Growth Factor Res.*, 5:37-54 (1994). Thus, it is likely that signal transduction pathways activated by KDR/FLK-1 include the ras pathway (Rozakis *et al.*, *Nature*, 360:689-692 (1992)), the PI-3'-kinase, the src-mediated and the pkγ-mediated pathways. Each of these pathways may play a critical role in the angiogenic and/or vasculogenic effect of KDR/FLK-1 in endothelial cells. Consequently, a still further aspect of this invention relates to the use of the organic compounds described herein to modulate angiogenesis and vasculogenesis as such processes are controlled by these pathways.

Conversely, disorders related to the shrinkage, contraction or closing of blood vessels, such as restenosis, are also implicated and may be treated or prevented by the methods of this invention.

Fibrotic disorders refer to the abnormal formation of extracellular matrices. Examples of fibrotic disorders include hepatic cirrhosis and mesangial cell proliferative disorders. Hepatic cirrhosis is characterized by the increase in extracellular matrix constituents resulting in the formation of a hepatic scar. An increased extracellular matrix resulting in a hepatic scar can also be caused by a viral infection such as hepatitis. Lipocytes appear to play a major role in hepatic cirrhosis. Other fibrotic disorders implicated include atherosclerosis.

Mesangial cell proliferative disorders refer to disorders brought about by abnormal proliferation of mesangial cells. Mesangial proliferative disorders include various human renal diseases such as glomerulonephritis, diabetic nephropathy and malignant nephrosclerosis as well as such disorders as thrombotic microangiopathy syndromes, transplant rejection, and glomerulopathies. The RTK PDGFR has been implicated in the maintenance of mesangial cell proliferation. Floege *et al.*, *Kidney International*, 43:47S-54S (1993).

Many cancers are cell proliferative disorders and, as noted previously, PKs have been associated with cell proliferative disorders. Thus, it is not surprising that PKs such as, for example, members of the RTK family have been associated with the development of cancer. Some of these receptors, like EGFR (Tuzi *et al.*, *Br. J. Cancer*, 63:227-233 (1991), Torp *et al.*, *APMIS*, 100:713-719 (1992)) HER2/neu (Slamon *et al.*, *Science*, 244:707-712 (1989)) and PDGF-R (Kumabe *et al.*, *Oncogene*, 7:627-633 (1992)) are over-expressed in many tumors and/or persistently activated by autocrine loops. In fact, in the most common and severe cancers these receptor over-expressions (Akbasak and Suner-Akbasak *et al.*, *J. Neurol. Sci.*, 111:119-133 (1992), Dickson *et al.*, *Cancer Treatment Res.*, 61:249-273 (1992), Korc *et al.*, *J. Clin. Invest.*, 90:1352-1360 (1992)) and autocrine loops (Lee and Donoghue, *J. Cell. Biol.*, 118:1057-1070 (1992), Korc *et al.*, *supra*, Akbasak and Suner-Akbasak *et al.*, *supra*) have been demonstrated. For example, EGFR has been associated with squamous cell carcinoma, astrocytoma, glioblastoma, head and neck cancer, lung cancer and bladder

cancer. HER2 has been associated with breast, ovarian, gastric, lung, pancreas and bladder cancer. PDGFR has been associated with glioblastoma and melanoma as well as lung, ovarian and prostate cancer. The RTK c-met has also been associated with malignant tumor formation. For example, c-met has been associated with, among other cancers, colorectal, thyroid, pancreatic, gastric and hepatocellular carcinomas and lymphomas. Additionally c-met has been linked to leukemia. Over-expression of the c-met gene has also been detected in patients with Hodgkins disease and Burkitts disease.

IGF-IR, in addition to being implicated in nutritional support and in type-II diabetes, has also been associated with several types of cancers. For example, IGF-I has been implicated as an autocrine growth stimulator for several tumor types, *e.g.* human breast cancer carcinoma cells (Arteaga *et al.*, *J. Clin. Invest.*, 84:1418-1423 (1989)) and small lung tumor cells (Macauley *et al.*, *Cancer Res.*, 50:2511-2517 (1990)). In addition, IGF-I, while integrally involved in the normal growth and differentiation of the nervous system, also appears to be an autocrine stimulator of human gliomas. Sandberg-Nordqvist *et al.*, *Cancer Res.*, 53:2475-2478 (1993). The importance of IGF-IR and its ligands in cell proliferation is further supported by the fact that many cell types in culture (fibroblasts, epithelial cells, smooth muscle cells, T-lymphocytes, myeloid cells, chondrocytes and osteoblasts (the stem cells of the bone marrow)) are stimulated to grow by IGF-I. Goldring and Goldring, *Eukaryotic Gene Expression*, 1:301-326 (1991). In a series of recent publications, Baserga suggests that IGF-IR plays a central role in the mechanism of transformation and, as such, could be a preferred target for therapeutic interventions for a broad spectrum of human malignancies. Baserga, *Cancer Res.*, 55:249-252 (1995), Baserga, *Cell*, 79:927-930 (1994), Coppola *et al.*, *Mol. Cell. Biol.*, 14:4588-4595 (1994).

STKs have been implicated in many types of cancer including, notably, breast cancer (Cance, *et al.*, *Int. J. Cancer*, 54:571-77 (1993)).

The association between abnormal PK activity and disease is not restricted to cancer. For example, RTKs have been associated with diseases such as psoriasis, diabetes mellitus, endometriosis, angiogenesis, atheromatous plaque development, Alzheimer's disease, von Hippel-Lindau disease, epidermal hyperproliferation, neurodegenerative diseases, age-related macular degeneration and hemangiomas. For example, EGFR has been indicated in corneal and dermal wound healing. Defects in Insulin-R and IGF-1R are indicated in type-II diabetes mellitus. A more complete correlation between specific RTKs and their therapeutic indications is set forth in Plowman *et al.*, *DN&P*, 7:334-339 (1994).

As noted previously, not only RTKs but CTKs including, but not limited to, src, abl, fps, yes, fyn, lyn, lck, blk, hck, fgr, AUR1, AUR2 and yrk (reviewed by Bolen *et al.*, *FASEB J.*, 6:3403-3409 (1992)) are involved in the proliferative and metabolic signal transduction pathway and thus could be expected, and have been shown, to be involved in many PTK-mediated disorders to which the present invention is directed. For example, mutated src (v-src) has been shown to be an oncoprotein ($pp60^{v\text{-}src}$) in chicken. Moreover, its cellular homolog, the proto-oncogene $pp60^{c\text{-}src}$ transmits oncogenic signals of many receptors. Over-expression of EGFR or HER2/neu in tumors leads to the constitutive activation of $pp60^{c\text{-}src}$, which is characteristic of malignant cells but absent in normal cells. On the other hand, mice

deficient in the expression of c-src exhibit an osteopetrotic phenotype, indicating a key participation of c-src in osteoclast function and a possible involvement in related disorders.

Similarly, Zap70 has been implicated in T-cell signaling which may relate to autoimmune disorders.

STKs have been associated with inflammation, autoimmune disease, immunoresponses, and hyperproliferation disorders such as restenosis, fibrosis, psoriasis, osteoarthritis and rheumatoid arthritis.

PKs have also been implicated in embryo implantation. Thus, the compounds of this invention may provide an effective method of preventing such embryo implantation and thereby be useful as birth control agents.

In yet another aspect, the compounds of the instant invention can also be used as anti-infective agents.

Finally, both RTKs and CTKs are currently suspected as being involved in hyperimmune disorders.

Pharmaceutical Compositions and Use

A compound of the present invention or a physiologically acceptable salt thereof, can be administered as such to a human patient or can be administered in pharmaceutical compositions in which the foregoing materials are mixed with suitable carriers or excipient(s). Techniques for formulation and administration of drugs may be found in "Remington's Pharmacological Sciences," Mack Publishing Co., Easton, PA, latest edition.

Routes of Administration

Suitable routes of administration may include, without limitation, oral, transoral, rectal, transmucosal or intestinal administration or intramuscular, epicutaneous, parenteral, subcutaneous, transdermal, intramedullary, intrathecal, direct intraventricular, intravenous, intravitreal, intraperitoneal, intranasal, intramuscular, intradural, intrarespiratory, nasal inhalation or intraocular injections. The preferred routes of administration are oral and parenteral.

Alternatively, one may administer the compound in a local rather than systemic manner, for example, via injection of the compound directly into a solid tumor, often in a depot or sustained release formulation.

Furthermore, one may administer the drug in a targeted drug delivery system, for example, in a liposome coated with tumor-specific antibody. The liposomes will be targeted to and taken up selectively by the tumor.

Composition/Formulation

Pharmaceutical compositions of the present invention may be manufactured by processes well known in the art, *e.g.*, by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping, lyophilizing processes or spray drying.

Pharmaceutical compositions for use in the methods of the present invention may be prepared by any methods of pharmacy, but all methods include the step of bringing in association the active ingredient with the carrier which constitutes one or more necessary ingredients. In particular,

pharmaceutical compositions for use in accordance with the present invention may be formulated in conventional manner using one or more physiologically acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. Proper formulation is dependent upon the route of administration chosen.

Dosage forms include tablets, troches, dispersions, suspensions, solutions, capsules, patches, syrups, elixirs, gels, powders, magmas, lozenges, ointments, creams, pastes, plasters, lotions, discs, suppositories, nasal or oral sprays, aerosols and the like.

For injection, the compounds of the invention may be formulated in aqueous solutions, preferably in physiologically compatible buffers such buffers with or without a low concentration of surfactant or cosolvent, or physiological saline buffer. For transmucosal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

For oral administration, the compounds can be formulated by combining the active compounds with pharmaceutically acceptable carriers well known in the art. Such carriers enable the compounds of the invention to be formulated as tablets, pills, lozenges, dragees, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient. Pharmaceutical preparations for oral use can be made using a solid excipient, optionally grinding the resulting mixture, and processing the mixture of granules, after adding other suitable auxiliaries if desired, to obtain tablets or dragee cores. Useful excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol, cellulose preparations such as, for example, maize starch, wheat starch, rice starch and potato starch and other materials such as gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinyl- pyrrolidone (PVP). If desired, disintegrating agents may be added, such as cross-linked polyvinyl pyrrolidone, agar, or alginic acid. A salt such as sodium alginate may also be used.

Dragee cores are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used which may optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for identification or to characterize different combinations of active compound doses.

Pharmaceutical compositions which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with a filler such as lactose, a binder such as starch, and/or a lubricant such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, liquid polyethylene glycols, cremophor, capmul, medium or long chain mono- di- or triglycerides. Stabilizers may be added in these formulations, also.

For administration by inhalation, the compounds for use according to the present invention are conveniently delivered in the form of an aerosol spray using a pressurized pack or a nebulizer and a suitable propellant, *e.g.*, without limitation, dichlorodifluoromethane, trichlorofluoromethane,

dichlorotetra- fluoroethane or carbon dioxide. In the case of a pressurized aerosol, the dosage unit may be controlled by providing a valve to deliver a metered amount. Capsules and cartridges of, for example, gelatin for use in an inhaler or insufflator may be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch.

The compounds may also be formulated for parenteral administration, *e.g.*, by bolus injection or continuous infusion. Formulations for injection may be presented in unit dosage form, *e.g.*, in ampoules or in multi-dose containers, with an added preservative. The compositions may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulating materials such as suspending, stabilizing and/or dispersing agents.

Pharmaceutical compositions for parenteral administration include aqueous solutions of a water soluble form, such as, without limitation, a salt, of the active compound. Additionally, suspensions of the active compounds may be prepared in a lipophilic vehicle. Suitable lipophilic vehicles include fatty oils such as sesame oil, synthetic fatty acid esters such as ethyl oleate and triglycerides, or materials such as liposomes. Aqueous injection suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers and/or agents that increase the solubility of the compounds to allow for the preparation of highly concentrated solutions.

Alternatively, the active ingredient may be in powder form for constitution with a suitable vehicle, *e.g.*, sterile, pyrogen-free water, before use.

The compounds may also be formulated in rectal compositions such as suppositories or retention enemas, using, *e.g.*, conventional suppository bases such as cocoa butter or other glycerides.

In addition to the formulations described previously, the compounds may also be formulated as depot preparations. Such long acting formulations may be administered by implantation (for example, subcutaneously or intramuscularly) or by intramuscular injection. A compound of this invention may be formulated for this route of administration with suitable polymeric or hydrophobic materials (for instance, in an emulsion with a pharmacologically acceptable oil), with ion exchange resins, or as a sparingly soluble derivative such as, without limitation, a sparingly soluble salt.

Alternatively, other delivery systems for hydrophobic pharmaceutical compounds may be employed. Liposomes and emulsions are well known examples of delivery vehicles or carriers for hydrophobic drugs. In addition, certain organic solvents such as dimethylsulfoxide also may be employed, although often at the cost of greater toxicity.

Additionally, the compounds may be delivered using a sustained-release system, such as semipermeable matrices of solid hydrophobic polymers containing the therapeutic agent. Various sustained-release materials have been established and are well known by those skilled in the art. Sustained-release capsules may, depending on their chemical nature, release the compounds for a few weeks up to over 100 days. Depending on the chemical nature and the biological stability of the therapeutic reagent, additional strategies for protein stabilization may be employed.

The pharmaceutical compositions herein also may comprise suitable solid or gel phase carriers or excipients. Examples of such carriers or excipients include, but are not limited to, calcium carbonate,

calcium phosphate, various sugars, starches, cellulose derivatives, gelatin, and polymers such as polyethylene glycols.

Many of the PK modulating compounds of the invention may be provided as physiologically acceptable salts wherein the claimed compound may form the negatively or the positively charged species. Examples of salts in which the compound forms the positively charged moiety include, without limitation, quaternary ammonium (defined elsewhere herein), salts such as the hydrochloride, sulfate, malate, carbonate, lactate, tartrate, maleate, succinate wherein the nitrogen atom of the quaternary ammonium group is a nitrogen of the selected compound of this invention which has reacted with the appropriate acid. Salts in which a compound of this invention forms the negatively charged species include, without limitation, the sodium, potassium, calcium and magnesium salts formed by the reaction of a carboxylic acid group in the compound with an appropriate base (*e.g.* sodium hydroxide (NaOH), potassium hydroxide (KOH), Calcium hydroxide ($Ca(OH)_2$), etc.).

Dosage

Pharmaceutical compositions suitable for use in the present invention include compositions wherein the active ingredients are contained in an amount sufficient to achieve the intended purpose, *i.e.*, the modulation of PK activity or the treatment or prevention of a PK-related disorder.

More specifically, a therapeutically effective amount means an amount of compound effective to prevent, alleviate or ameliorate symptoms of disease or prolong the survival of the subject being treated.

Determination of a therapeutically effective amount is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein.

For any compound used in the methods of the invention, the therapeutically effective amount or dose can be estimated initially from cell culture assays. Then, the dosage can be formulated for use in animal models so as to achieve a circulating concentration range that includes the IC_{50} as determined in cell culture (*i.e.*, the concentration of the test compound which achieves a half-maximal inhibition of the PK activity). Such information can then be used to more accurately determine useful doses in humans.

Toxicity and therapeutic efficacy of the compounds described herein can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, *e.g.*, by determining the IC_{50} and the LD_{50} (both of which are discussed elsewhere herein) for a subject compound. The data obtained from these cell culture assays and animal studies can be used in formulating a range of dosage for use in humans. The dosage may vary depending upon the dosage form employed and the route of administration utilized. The exact formulation, route of administration and dosage can be chosen by the individual physician in view of the patient's condition. (See *e.g.*, Fingl, *et al.*, 1975, in "The Pharmacological Basis of Therapeutics", Ch. 1 p.1).

Dosage amount and interval may be adjusted individually to provide plasma levels of the active species which are sufficient to maintain the kinase modulating effects. These plasma levels are referred to as minimal effective concentrations (MECs). The MEC will vary for each compound but can be estimated from *in vitro* data, *e.g.*, the concentration necessary to achieve 50-90% inhibition of a kinase may be ascertained using the assays described herein. Dosages necessary to achieve the MEC will

depend on individual characteristics and route of administration. HPLC assays or bioassays can be used to determine plasma concentrations.

Dosage intervals can also be determined using MEC value. Compounds should be administered using a regimen that maintains plasma levels above the MEC for 10-90% of the time, preferably between 30-90% and most preferably between 50-90%. At present, the therapeutically effective amounts of the inventive compounds described herein may range from approximately 25 mg/m^2 to 1000- mg/m^2 perday. Even more preferably 25 mg/m^2 to 150 mg/m^2.

In cases of local administration or selective uptake, the effective local concentration of the drug may not be related to plasma concentration and other procedures known in the art may be employed to determine the correct dosage amount and interval.

The amount of a composition administered will, of course, be dependent on the subject being treated, the severity of the affliction, the manner of administration, the judgment of the prescribing physician, etc.

Packaging

The compositions may, if desired, be presented in a pack or dispenser device, such as an FDA approved kit, which may contain one or more unit dosage forms containing the active ingredient. The pack may for example comprise metal or plastic foil, such as a blister pack. The pack or dispenser device may be accompanied by instructions for administration. The pack or dispenser may also be accompanied by a notice associated with the container in a form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals, which notice is reflective of approval by the agency of the form of the compositions or of human or veterinary administration. Such notice, for example, may be of the labeling approved by the U.S. Food and Drug Administration for prescription drugs or of an approved product insert. Compositions comprising a compound of the invention formulated in a compatible pharmaceutical carrier may also be prepared, placed in an appropriate container, and labeled for treatment of an indicated condition. Suitable conditions indicated on the label may include treatment of a tumor, inhibition of angiogenesis, treatment of fibrosis, diabetes, and the like.

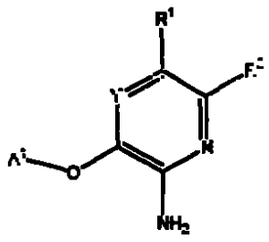
EXAMPLES

The following examples are given to illustrate the present invention. It should be understood, however, that the invention is not to be limited to the specific conditions or details described in these examples.

The numbering in the examples corresponds to the numbering in the Tables herein. Reaction schemes and example numbers beginning with a letter (I) relate to pyridine compounds, whereas those beginning with a letter (II) relate to pyrazine compounds. Example numbers beginning with L are library syntheses. Example numbers having a letter notation (a, b, c, etc.) illustrate the synthesis of reagents subsequently used in the synthesis of the inventive compounds, which have a number notation (1, 2, 3, etc.). Reagents can be synthesized as shown herein, or are available from commercial sources (e.g., Aldrich, Milwaukee, WI; Acros, Morris Plains, NJ; Biosynth International, Naperville, IL; Frontier Scientific, Logan, UT; TCI America, Portland, OR; Combi-Blocks, San Diego, CA; Matrix Scientific, Columbia, SC; Acros, Morris Plains, NJ; Alfa Aesar, Ward Hill, MA; Apollo Scientific, UK; etc.) or can be

synthesized by procedures known in the art. When a general or exemplary synthetic procedure is referred to, one skilled in the art can readily determine the appropriate reagents, if not indicated, extrapolating from the general or exemplary procedures.

In the general procedures 1-43 described herein, although some of the procedures are generalized and exemplary, past tense is used to indicate that these general procedures were the procedures used to synthesize the compounds. Some of the general procedures are given as examples for preparing specific compounds. One skilled in the art can readily adapt such procedures to the synthesis of other compounds. It should be understood that R groups shown in the general procedures are meant to be generic and non-limiting, and do not correspond to definitions of R groups elsewhere in this document. Each such R group represents one or multiple chemical moieties that can be the same or different from other chemical moieties also represented by the same R symbol. Moreover, representation of an unsubstituted position in structures shown or referred to in the general procedures is for convenience and does not preclude substitution as described elsewhere herein. For specific groups that can be present, either as R groups in the general procedures or as optional substitutents not shown, refer to the descriptions in the remainder of this document, including the claims, summary and detailed description. It should be further understood that compound numbers shown in the general schemes and general procedures in the Examples are for convenient reference only, and do not correspond to the numbers used elsewhere throughout this document. For example, the nitropyridine compound (1) in general scheme I is different from the compound of formula 1

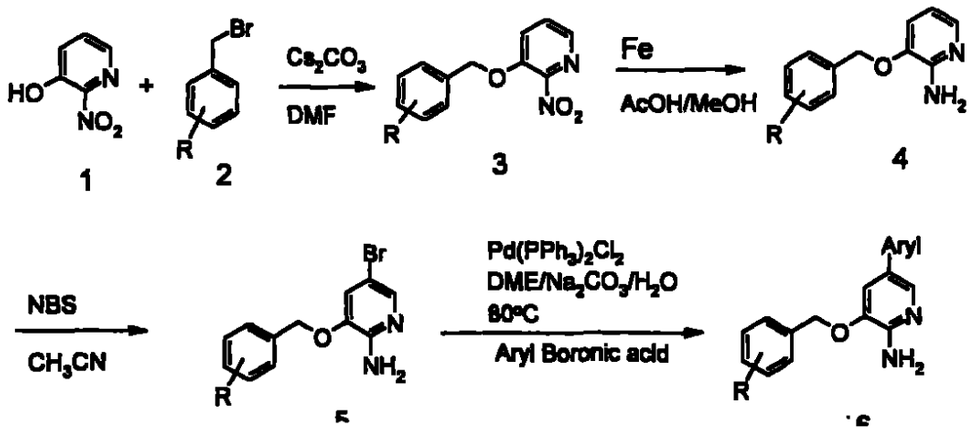


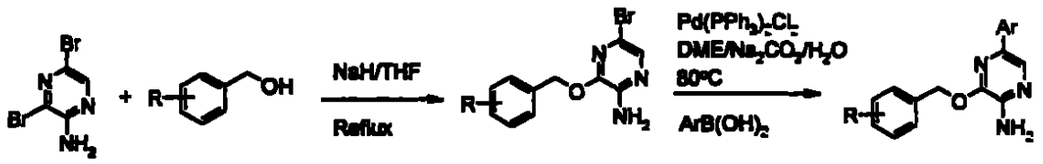
1

described herein.

General Scheme I for the Synthesis of 5-Aryl-3-(Substituted-Benzyloxy)-Pyridin-2-ylamine (6):

General Scheme II for the Synthesis of 5-Aryl-3-(Substituted-Benzyloxy)-Pyrazin-2-ylamine





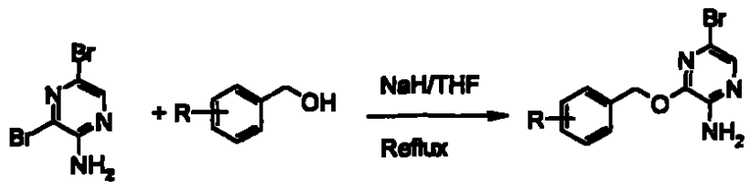
General Procedure 1 for the Synthesis of 5-Bromo-3-(Substituted-Benzyloxy)-Pyridin-2-ylamine (5):

1. Preparation of 3-(substituted-benzyloxy)-2-nitro-pyridine (3): To a stirred solution of Cs_2CO_3 (1.0 molar equivalent)) in DMF (0.2 M) under a N_2 atmosphere containing 3-hydroxy-4-nitro-pyridine (Aldrich, 1.0 molar equivalent) was added substituted benzyl bromide (1.0 molar equivalent). The mixture was stirred for 6 h at ambient temperature. The reaction was then diluted with EtOAc , and partitioned with H_2O. The aqueous layer was extracted with EtOAc twice. The organic layers were then combined, washed with H_2O and brine, dried over Na_2SO_4, filtered, and concentrated to dryness under vacuum to yield 3-(substituted-benzyloxy)-2-nitro-pyridine (3) as a solid.

2. Preparation of 3-(substituted-benzyloxy)-pyridin-2-ylamine (4): To a stirred mixture of AcOH and EtOH (1.3:1) was suspended 3-(substituted-benzyloxy-2-nitro-pyridine (1.0 molar equivalent, 1 M) and iron chips (1.0 molar equivalent). The reaction was heated slowly to reflux and allowed to stir for 1 hr. The reaction was cooled to room temperature then filtered through a pad of celite. The resulting filtrate was neutralized with conc. NH_4OH, and then extracted with EtOAc for three times. The combined organic extracts were washed with saturated $NaHCO_3$, H_2O, and brine, dried over Na_2SO_4, filtered and concentrated to dryness under vacuum to yield 3-(substituted-benzyloxy)-pyridin-2-ylamine (4) as a solid.

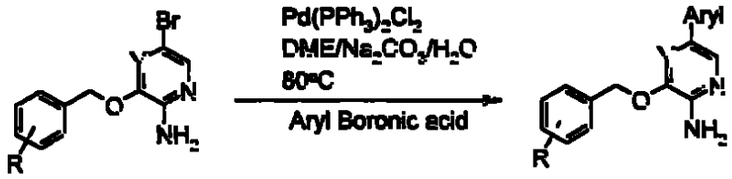
3. Preparation of 5-bromo-3-(substituted benzyloxy)-pyridin-2-ylamine (5): A stirring solution of 3-(substituted-benzyloxy)-pyridin-2-ylamine (4) (1.0 molar equivalent) in acetonitrile was cooled to 0 °C using an ice bath. To this solution was added *N*-bromosuccinimide (Aldrich, 1.0 molar equivalent) portionwise. The reaction was stirred at 0°C for 15 min. The reaction was concentrated to dryness under vacuum. The resulting dark oil was dissolved in EtOAc and partitioned with H_2O. The organic was then washed with saturated $NaHCO_3$ twice and brine once. Activated charcoal was added to the organic layer and warmed to reflux. The solution was then cooled to room temperature and filtered through a pad of celite. The organic was then concentrated to dryness under vacuum to one third the original volume. The solids were then filtered off to yield 5-bromo-3-(substituted benzyloxy)-pyridin-2-ylamine (5) as a solid.

General Procedure 2 for the Synthesis of 5-Bromo-3-(Substituted-Benzyloxy)-Pyrazin-2-ylamine.



To an ice cooled solution of substituted benzyl alcohol (1.0 molar equivalent) and anhydrous tetrahydrofuran (0.14 M) was added sodium hydride (1.0 molar equivalent) slowly under nitrogen atmosphere. After stirring for 30 minutes, 3,5-dibromopyrazin-2-ylamine (1.0 molar equivalent) in tetrahydrofuran (0.56 M) was added via an addition funnel at a fast dropwise rate. Once the addition was complete the ice bath was removed and the reaction was refluxed under nitrogen and monitored by reversed phase HPLC. After 18 hr HPLC showed that the majority of the starting 3,5-dibromopyrazin-2-ylamine had been consumed and the reaction was allowed to cool to room temperature. The reaction mixture was concentrated, diluted with ethyl acetate, and washed with brine. The organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuum. The crude product was purified using a silica gel eluting with 1:1 ethyl acetate/dichloromethane to yield the 5-bromo-3-(substituted-benzyloxy)-pyrazin-2-ylamine as a white solid in 60-90% yield.

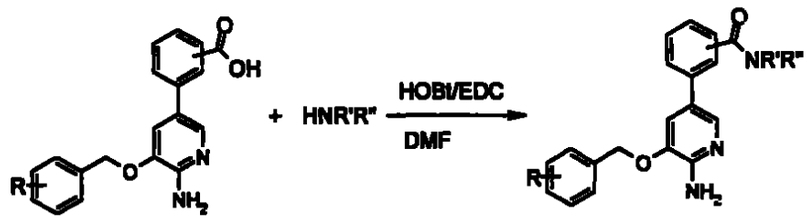
General Procedure 3 for the Synthesis of 5-Aryl-3-(Substituted-Benzyloxy)-Pyridin-2-ylamine and 5-Aryl-3-(Substituted-Benzyloxy)-Pyrazin-2-ylamine.



Y: CH or N

A mixture of 5-bromo-3-(substituted-benzyloxy)-pyridin-2-ylamine or 5-bromo-3-(substituted-benzyloxy)-pyrazin-2-ylamine (1 molar equivalent), aryl boronic acid or ester (1.2 molar equivalent), bis(triphenylphosphine) palladium II chloride (0.03 molar equivalent) and sodium carbonate (3.0 molar equivalent) in ethylene glycol dimethyl ether and water (10:0.5, 0.03 M) was de-gassed and charged with nitrogen for three times, and then heated to reflux under nitrogen for overnight. The reaction was cooled to ambient temperature and diluted with ethyl acetate. The mixture was washed with water, brine, dried over Na_2SO_4, and purified on a silica gel column to afford 5-aryl-3-(substituted-benzyloxy)-pyridin-2-ylamine, or 5-aryl-3-(substituted-benzyloxy)-pyrazin-2-ylamine.

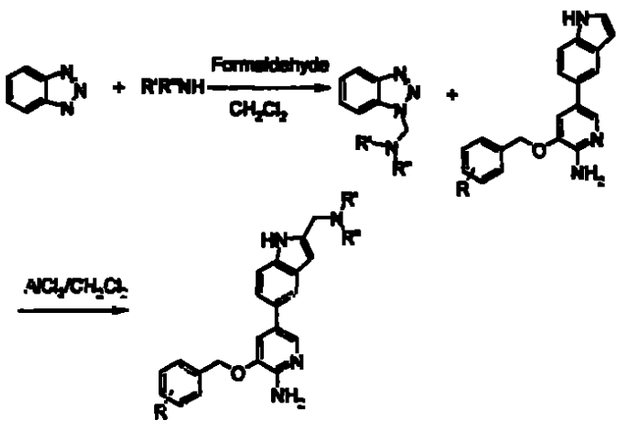
General Procedure 4 for Amidation Reaction of 6-amino-5-(substituted-benzyloxy)-pyridin-3-yl]-benzoic acid:



To a solution of 6-amino-5-(substituted-benzyloxy)-pyridin-3-yl]-benzoic acid (1 molar equivalent), 1-hydroxybenzotriazole hydrate (HOBT, 1.2 molar equivalent), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC, 1.2 molar equivalent) in DMF (0.2 M) was added amine (1.2 molar equivalent). The reaction solution was stirred at room temperature for

overnight, then diluted with EtOAc, and partitioned with H_2O. The organic was separated and the aqueous was extracted with EtOAc. The organic layers were combined, washed with saturated $NaHCO_3$, and concentrated to dryness under vacuum. The material was purified using column chromatography (silica gel, 99:1 to 95:5 CH_2Cl_2/MeOH). The fractions containing product were concentrated under vacuum to yield the amide product.

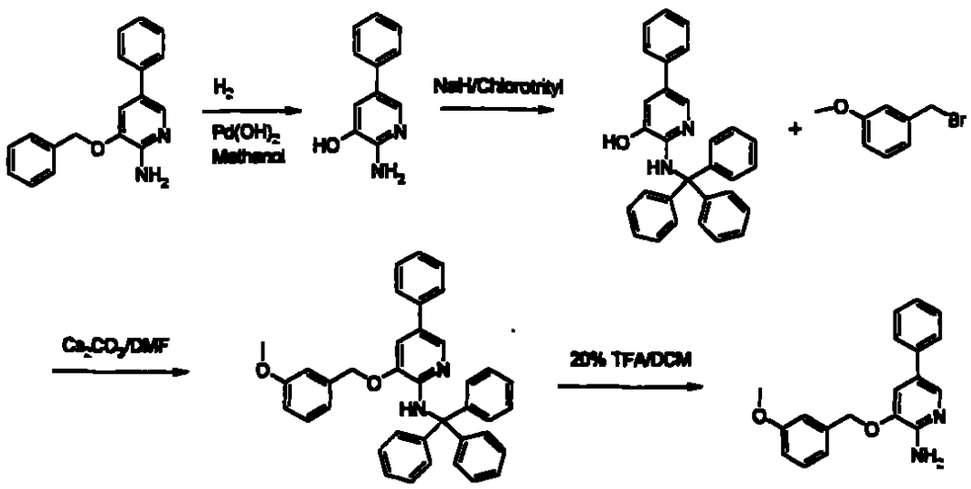
General procedure 5 for the preparation of 3-(substituted-benzyloxy)-5-(3-dialkylaminomethyl-1*H*-indol-5-yl)-pyridin-2-ylamine:



To a solution of benzotriazole (1.0 molar equivalent) in dichloromethane (0.2 M) was added amine (1.0 molar equilvalent). The reaction was stirred for 5 minutes at room temperature after which formaldehyde (37 % by wt, 1.0 molar equivalent) was added and the reaction was capped and stirred at room temperature for 3 hr. Once TLC (10 % ethyl acetate: dichloromethane) showed the consumption of starting benzotriazole the reaction was dried with anhydrous magnesium sulfate (10 g), filtered and concentrated in vacuo. The crude product was purified with a silica gel column eluting with 1:1 ethyl acetate: dichloromethane to yield the desired product as a white solid.

To a solution of the aminomethylbenzotriazole intermediate (1.0 molar equivalent) in dichloromethane (0.43 M) was added aluminum chloride (2.0 molar equivalent), and then followed by 3-(2,6-Dichloro-benzyloxy)-5-(1*H*-indol-5-yl)- pyridine-2-ylamin (1.1 molar equivalent). The reaction was capped and heated with stirring to 40°C for 3-4 hr. The reaction was then removed from the heat and allowed to cool to room temperature. The reaction mixture was diluted with sodium hydroxide (0.2 M) and chloroform, recapped and vigorously stirred at room temperature to dissolve the residue in the vial. The chloroform was extracted away from the aqueous, dried over anhydrous sodium sulfate and concentrated in vacuo. The crude product was purified with a silica gel column, first eluting with 1:1, ethyl acetate: dichloromethane, to elute the less polar impurities and then eluting the product with 90:9:1, chloroform:methanol:ammonium hydroxide. (Yields 10-67%.)

General Procedure 6 for the synthesis of 3-(Substituted-benzyloxy)-5-phenyl-pyridin-2-ylamine using example I-88:

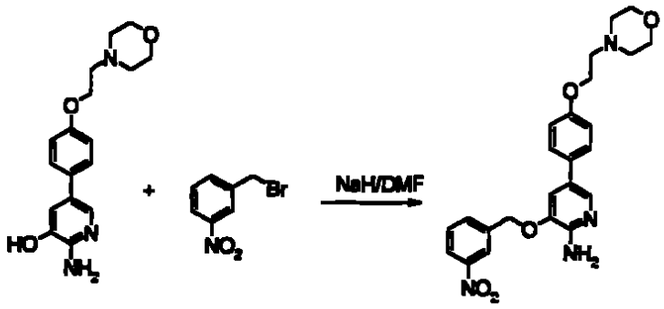


To a solution of 3-benzyloxy-5-phenyl-pyridin-2-ylamine (Example I-87, 3.27g, 11.8mmol) in methanol (30mL) was added $Pd(OH)_2$ (2.5g, 2.37mmol). The mixture was degassed and charged with hydrogen three times, and then stirred under hydrogen balloon for 5 hr. The reaction was filtered through a celite pad, washed with methanol, and condensed. After high vacuum dry, 2-amino-5-phenyl-pyridin-3-ol was obtained (2.04g, 93% yield). MS *m/z* 187 [M+1].

To a solution of 2-amino-5-phenyl-pyridin-3-ol (2.04 g, 10.95 mmol) in THF (anhydrous, 30 mL) was added NaH (1.31 g, 32.85 mmol) slowly. The mixture was stirred under nitrogen for 20 minutes, and then trityl chloride (3.66 g, 13.14 mmol) was added. The reaction was stirred at room temperature for over night under nitrogen. The solvent was evaporated, and the residue was dissolved in dichloromethane, washed with water, and dried over Na_2SO_4. After filtration and condensation, the crude product was purified on a silica gel column eluting with EtOAc-Hexane (1:10) to provide 5-phenyl-2-(trityl-amino)-pyridin-3-ol (1.09 g, 23% yield). MS *m/z* 427 [M+1].

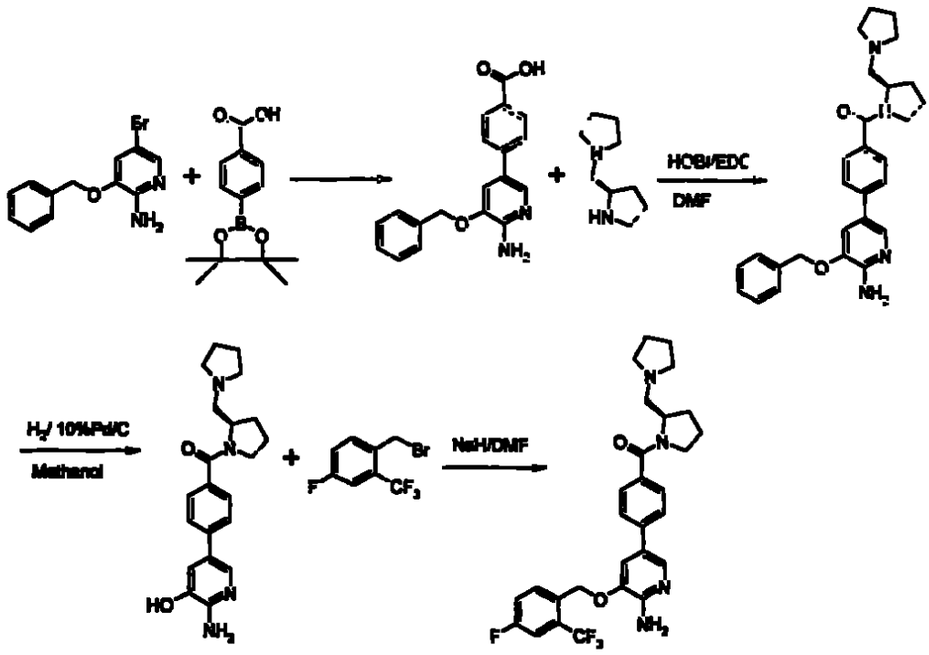
To a solution of 5-phenyl-2-(trityl-amino)-pyridin-3-ol (100 mg, 0.24 mmol) in THF (3 mL) was added Cs_2CO_3 (79 mg, 0.24 mmol). The mixture was stirred at room temperature for 20 minutes, and then 3-methoxybenzylbromide (0.037 mL, 0.26 mmol) was added. The reaction was stirred at room temperature overnight, diluted with dichloromethane (5 mL), and filtered to remove the salts. The solvents were evaporated, and the residue was dissolved in 10% trifluoroacetic acid in dichloromethane (2 mL). The reaction was stirred for 2 hr, and evaporated. The residue was dissolved in dichloromethane, washed by sat. $NaHCO_3$, and dried over Na_2SO_4. After filtration and concentration, the crude product was purified on a silica gel column eluting with methanol-dichloromethane (from 3% to 15% gradient) to provide 3-(3-methoxy-benzyloxy)-5-phenyl-pyridin-2-ylamine as a white solid (43.5 mg, 60% yield).

General Procedure 7 for the Synthesis of 3-(Substituted-benzyloxy)-5-Aryl-pyridin-2-ylamine using Example I-106:



To a solution of 2-amino-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-3-ol (prepared according to the procedures for 2-amino-5-phenyl-pyridin-3-ol in Example I-88) (45.5 mg, 0.14 mmol) in DMF (3 mL) at 0°C was added NaH (60% in oil) (5.6 mg, 0.14 mmol) and the mixture was stirred at 0°C for 20 min. Then 1-Bromomethyl-3-nitro-benzene was added and the mixture was stirred at 0°C for 1 hr and at room temperature for 2hr. Cold 1 N aqueous HCl (0.1 mL) was added and the solvent was removed under reduced pressure. The residue was purified with silica gel chromatography (CH_2Cl_2:MeOH:NH_4OH = 100:3:0.3) to give 5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-3-(3-nitro-benzyloxy)-pyridin-2-ylamine as yellow solid (44 mg, 68%).

General Procedure 8 for the Synthesis of {4-[6-Amino-5-(substituted-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone using Example I-111:



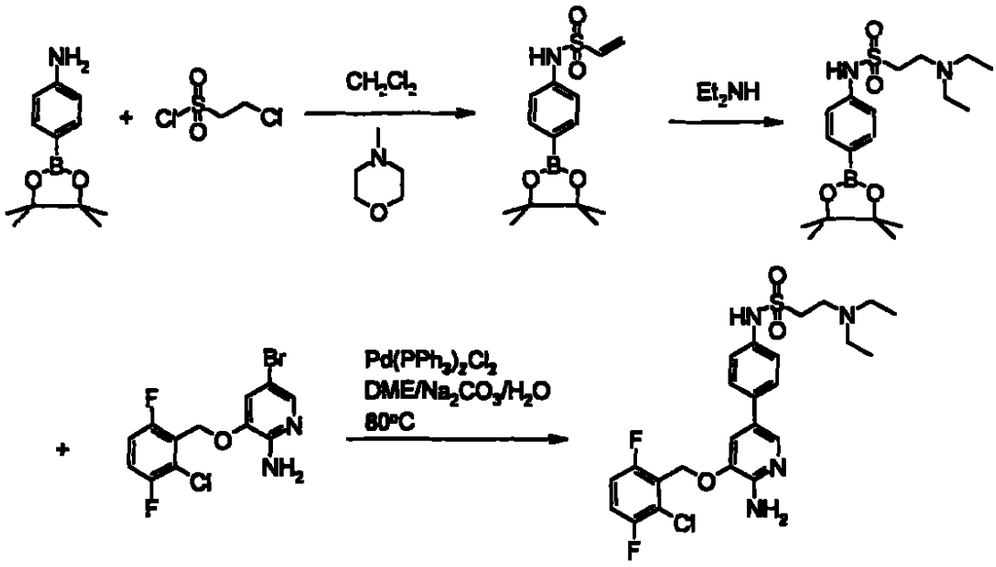
1. 6-Amino-5-benzyloxy-nicotinic acid was prepared according to procedure 3 from 3-benzyloxy-5-bromo-pyridin-2-ylamine and 4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzoic acid. MS *m/z* 321 (M+1).

2. [4-(6-amino-5-benzyloxy-pyridin-3-yl)-phenyl]-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone was prepared following procedure 4 using 6-amino-5-benzyloxy-nicotinic acid and (2*R*)-pyrrolidin-1-ylmethyl-pyrrolidine (prepared in Example I-39). MS *m/z* 457 (M+1).

3. To a solution of [4-(6-amino-5-benzyloxy-pyridin-3-yl)-phenyl]-[(2*R*)-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone (2.28 g, 5.00 mmol) in methanol (25 mL) was added 10% Pd/C (100 mg). The mixture was degassed and charged with hydrogen for three times, and then stirred under hydrogen balloon overnight. The reaction was filtered through a celite pad, washed with methanol, and condensed. After high vacuum dry, [4-(6-amino-5-hydroxy-pyridin-3-yl)-phenyl]-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone was obtained (1.74 g, 95% yield). ^{1}H NMR(400 MHz, DMSO-d_6) δ 7.79 (s, 1H), 7.54 (m, 3H), 7.46 (m, 2H), 7.14 (s, 1H), 5.68 (s, 2H), 4.22 (m, 1H), 3.45 (m, 2H), 2.68 (m, 1H), 2.52 (m, 4H), 1.96 (m, 2H), 1.84 (m, 3H), 1.64 (m, 4H); MS *m/z* 367 (M+1).

4. To a stirred solution of [4-(6-amino-5-hydroxy-pyridin-3-yl)-phenyl]-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone (100 mg, 0.27mmol) in anhydrous DMF(15 mL) under a N_2 atmosphere containing, at 0°C, sodium hydride (60% dispersion in mineral oil, 11 mg, 0.49mmol) was added . The mixture was allowed to stir at 0°C for 30 min. 1-(Bromomethyl)-4-fluoro-2-(trifluoromethyl)benzene (0.046 mL, 0.27mmol) was added. The mixture was stirred at room temperature for 2hr.The reaction was diluted with EtOAc, and partitioned with H_2O. The aqueous layer was extracted with EtOAc (2 x 25 mL). The organic layers were combined, washed with H_2O (1 x 15mL), brine (1 x 15mL), dried over $MgSO_4$, filtered, concentrated, and purified on a silica gel column to yield {4-[6-amino-5-(4-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone as off-white crystals.

General Procedure F for the Synthesis 2-Dialkylamino-ethanesulfonic acid [6-amino-5-(substituted-benzyloxy)-pyridin-3-yl]-phenyl-amide using Example I-243.



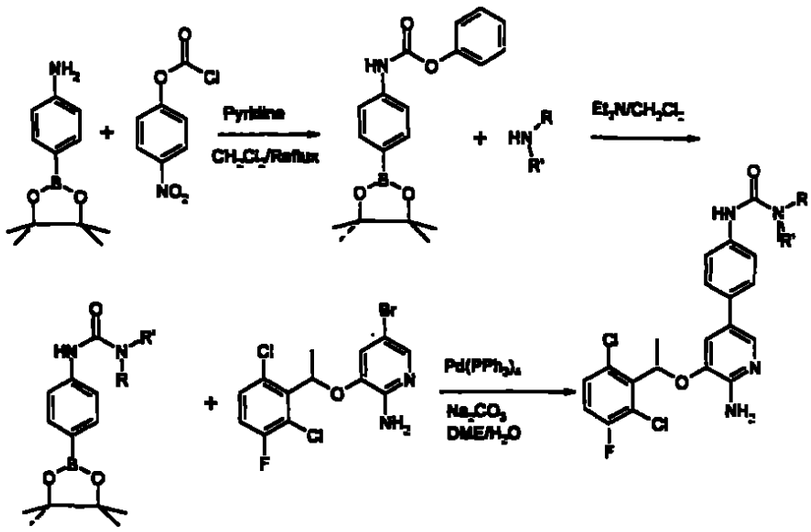
1. To a solution of 4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenylamine (5 g, 22.8 mmol) in dichloromethane (120 mL) was added *N*-methyl morpholine (7.5 mL, 68.4 mmol). This mixture was cooled to 0°C under nitrogen atmosphere. 2-Chloroethanesulfonyl chloride (2.5 mL, 23.9 mmol) in dichloromethane (60 mL) was then added drop wise with stirring. Once the addition was complete the flask was stirred at 0°C for 1 hr and then at room temperature while monitoring by TLC (1:1 ethyl acetate:hexanes) and staining with ninhydrin. After 4 h stirring some starting boronic ester still remained and an additional 0.2 equivalents (0.5 mL) of 2-chloroethanesulfonyl chloride in dichloromethane (25 mL) was added drop wise at room temperature. After 1 hr the boronic ester had been consumed as shown by TLC and the total reaction volume was reduced by one-half via rotary evaporation. The contents were diluted with ethyl acetate (200 mL), washed with 50% brine (2 x 100 mL), dried over anhydrous sodium sulfate and concentrated in vacuum. The crude product was purified using silica gel (120 g) and eluting with 10% ethyl acetate, dichloromethane to yield ethenesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amides as a white solid (6.2 g, 20.2 mmol, 89% yield). ^{1}H NMR ($CDCl_3$, 300 MHz), δ 7.76 (d, J = 8.4, 2H), 7.12 (d, J = 8.45, 2H) 6.65 (s, 1H), 6.55 (dd, J = 9.77, 6.7, 1H), 6.31 (d, J = 16.54, 1H), 5.96 (d, J = 9.8, 1H), 1.33 (s, 12H).

2. To a solution of ethenesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (0.500 g, 1.6 mmol) in methanol (5 mL) was added diethylamine (0.707 g, 4.0 mmol) in methanol (5 mL), and the reaction was stirred at room temperature and monitored by TLC (1:1 Ethyl acetate: hexanes). After 2 hr the reaction was concentrated in vacuum and the residue partitioned between ethyl acetate (50 mL) and water (50 mL). The ethyl acetate was then washed with 50% brine (1 x 50 mL), dried over anhydrous sodium sulfate, filtered and concentrated in vacuum. Crude product was purified using a 10 g prepacked silica gel column, eluting with 1:1 ethyl acetate: dichloromethane to provide 2-diethylamino-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide as a white solid (0.346 g, 0.90 mmol, 56%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.78 (d, J = 6.65, 2H) 7.15 (d, J = 6.66, 2H), 3.20 (m, 2H), 3.0 (m, 2H), 2.55 (q, J = 7.15, 7.16 4H), 1.34 (s, 12H), 1.05 (t, J = 7.19, 6H).

3. 2-diethylamino-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide was prepared following the general Suzuki coupling procedure 3 from 5-bromo-3-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-2-ylamine and 2-diethylamino-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide prepared in part 2 as a white solid in 60% yield.

General Procedure 10:

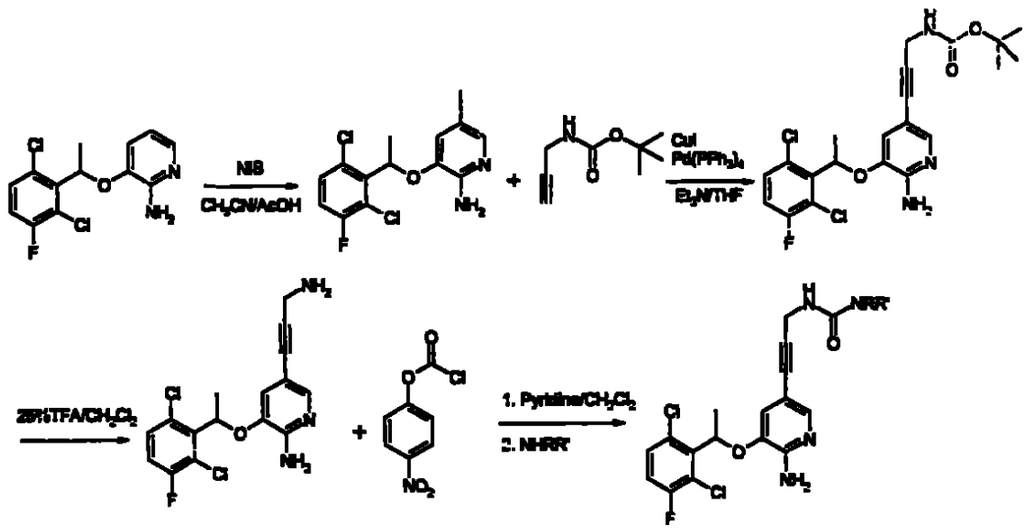
1: 4-(4,4,5,5-tetramethyl 1,3,2 dioxaborolan-2-yl) aniline (3 g, 0.013 mol) was dissolved in dichloromethane (350 mL) to which pyridine (1.02 g, 0.013 mol) and 4-nitrophenyl chloroformate was added. The reaction was stirred for 13 hr where TLC analysis showed consumption of all starting materials. The solution was washed with saturated $NaHCO_3$ (3 x 50 mL), water (3 x 50 mL) and brine (3 x 50 mL). The organic layer was dried over Na_2SO_4 and solvent removed to yield a white crystalline solid [4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-carbamic acid phenyl ester, 4.45 g, 91%. ^{1}H NMR ($CDCl_3$ 300 MHz) δ 1.4 (s, 12H), 7.1 (brs, 1H), 7.3 (d, 2H), 7.5 (d, 2H), 7.8 (d, 2H), 8.3 (d, 2H).



2: [4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-carbamic acid phenyl ester (500 mg, 1.3 mmol) was dissolved in anhydroue dichloromethane (0.5 mL) and triethylamine (0.167 mL, 1.3 mmol). To this stirred solution was added 1-methyl piperazine (or any other amine) (0.144 mL, 1.3 mmol). The solution turned yellow instantly, and tlc analysis showed consumption of all starting material. The reaction was washed with water (3 x 500 mL), saturated sodium bicarbonate (2 x 200 mL) and dried prior to removal of solvents in vacuo. The boronic esters were used without purification.

3: To a mixture of 2.1 mL of DME and 2.8 mL of 2N Na_2CO_3 was added 100 mg of the bromide scaffold, 1 equivalent of the boronic acid, and 5 mol % of $Pd(PPh_3)_4$. The reaction was stirred and heated at 80°C overnight in a two dram vial. The crude mixture was filtered through celite and extracted with EtOAc (2 x 100 mL). The combined extracts were washed with $NaHCO_3$ (1 x 100 mL), followed by water (1 x 100 mL), and then saturated brine (1x 100mL). The resulting mixture was concentrated in vacuum. The residue was dissolved in hexane and purified via column chromatography.

General Procedure 11:



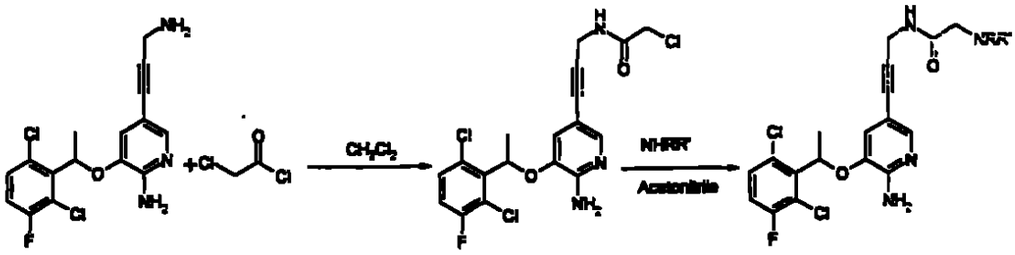
1: To a solution of 3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine (10.0 g, 33.2 mmol) in acetonitrile (600 mL) and acetic acid (120 mL) was added N-Iodosuccinimide (11.2 g, 49.8 mmol). The mixture was stirred at room temperature for 4 hr and the reaction was quenched with $Na_2S_2O_5$ solution. After evaporation, the residue was partitioned between ethyl acetate and water. The organic layer was washed with 2N NaOH solution, brine, and dried over Na_2SO_4. The crude product was purified on a silica gel column to provide 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-Iodo-pyridin-2-ylamine (7.1 g, 50% yield).MS *m/z* 427 [M+1]

2: To a solution of 3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-Iodo-pyridin-2-ylamine (7.1 g, 16.6 mmol) and prop-2-ynyl-carbamic acid tert-butyl ester (3.1 g, 20.0 mmol) in THF (60 mL) and Et_3N (60 mL) was added CuI (63 mg, 0.3 mmol) and $Pd(PPh_3)_4$ (364 mg, 0.3 mmol). The mixture was stirred under nitrogen and monitored by TLC until the reaction was complete. The mixture was extracted with EtOAc and washed by water. The crude product was purified on a silica gel column eluting with 20-40% EtOAc in hexanes to provide (3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-carbamic acid tert-butyl ester (2.2 g, 28% yield).

3: The solution of (3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-carbamic acid tert-butyl ester in 25% TFA in dichloromethane was stirred for 2 hr, then washed by 2N NaOH, water twice, brine, dried over Na_2SO_4. After filtration and evaporation, 5-(3-amino-prop-1-ynyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine was obtained in 93% yield.

4: To a solution of 5-(3-amino-prop-1-ynyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine (0.282 mmol, 1 eq) and 4-nitrophenyl chloroformate (1 eq) in anhydrous dichloromethane (10 mL) was added pyridine (1 eq). The reaction was stirred for 4 hr under nitrogen, and then the selected amine (1 eq) and triethylamine (1 eq) were added. The mixture was refluxed for 5 minutes and cooled to room temperature. The reaction mixture was washed with water. The organic layer was evaporated and purified on a silica gel column eluting with 0-20% methanol in dichloromethane on prepacked silica columns. Final yields varied between 24% and 71%.

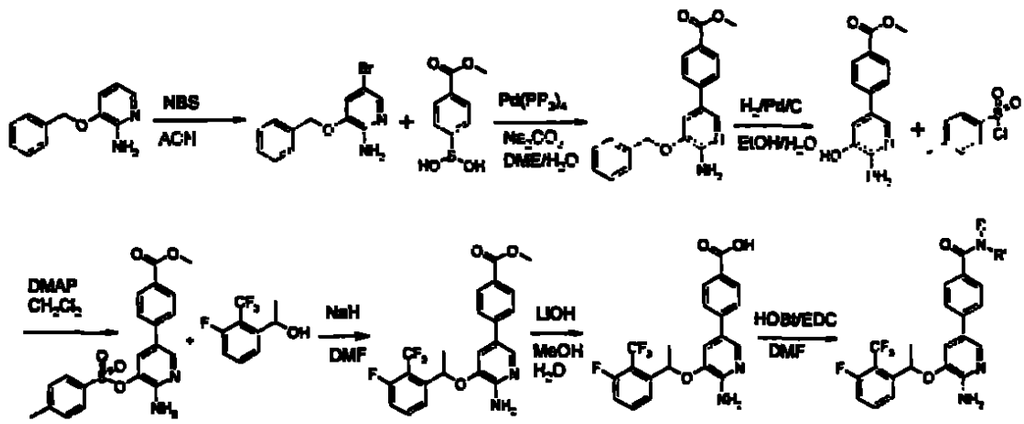
<u>General Procedure 12</u>:



1: To a solution of 5-(3-amino-prop-1-ynyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine (prepared in procedure 11) (400 mg, 1.1 mmol) in dichloromethane (17 mL) was added chloroacetyl chloride (153 mg, 1.4 mmol). The reaction was stirred at room temperature with TLC monitor of the completion of the reaction. After the completion, the solvent was evaporated to get the crude product.

2: To a solution of N-(3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-2-chloro-acetamide (1 eq) in acetonitrile (5 eq) was added the individual amine (5 eq). The mixture was refluxing under nitrogen overnight. After evaporation of solvent, the residue was purified on a silica gel column eluting with 1-10% methanol in dichloromethane to provide the product with yields varied between 47% to 97%.

General Procedure 13:



1. To a stirred solution of 2-amino-3-benzyloxypyridine (42.0 g, 0.21 mol) in CH_3CN (600 mL) at 0°C was added N-bromosuccinimide (37.1 g, 0.21 mol) over 30 minutes. The mixture was stirred for 0.5 hr, after which the reaction was then diluted with EtOAc (900 mL) and partitioned with H_2O (900 mL). The organic layer was washed with brine and dried (Na_2SO_4), filtered and concentrated to dryness under vacuum to yield 3-benzyloxy-5-bromo-pyridin-2-ylamine (31.0 g, 0.11 mol, 53%). ^1H NMR ($CDCl_3$, 300 MHz) δ 4.63-4.78 (brs, 2H), 5.04 (s, 2H), 7.07 (d, 1H, *J*, 1.8 Hz), 7.33-7.42 (m, 5H), 7.73 (d, 1H, *J*, 1.8 Hz).

2. To a stirred mixture of 3-benzyloxy-5-bromo-pyridin-2-ylamine (31.0 g, 0.11 mol) in a mixture of DME (600 mL) and H_2O (600 mL) was added 4-carboxymethylboronic acid (29.9 g, 0.11 mol), $Pd(PPh_3)_4$ (6.4 g, 5.55 mmol), and Na_2CO_3 (82.0 g, 0.78 mol). The reaction was heated slowly to reflux and allowed to stir for 3 hr. The reaction was cooled to room temperature, then diluted with CH_2Cl_2 (1.5

L) and partitioned with H_2O (700 mL). The organic layer was washed with saturated $NaHCO_3$ (700 mL), dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude material was purified by column chromatography (silica gel, 1:1 to 4:1 EtOAc:hexanes) and the fractions containing product were combined and concentrated in vacuo to yield 4-(6-amino-5-benzyloxy-pyridin-3-yl)-benzoic acid methyl ester (29.4 g, 0.086 mol, 79%). ^1H NMR ($CDCl_3$, 300 MHz) δ 3.92 (s, 3H), 4.82-4.94 (brs, 2H), 5.15 (s, 2H), 7.22 (d, 1H, *J*, 1.8 Hz), 7.33-7.42 (m, 5H), 7.54 (d, 2H, *J*, 8.6), 7.98 (d, 1H, *J*, 1.8 Hz), 8.06(d, 2H, *J*, 8.6 Hz).

3. To a stirring solution of 4-(6-amino-5-benzyloxy-pyridin-3-yl)-benzoic acid methyl ester (10.0 g, 0.03 mol) in EtOH:H_2O (95:5, 600 mL) was added Pd/C (15.9 g, 0.015 mol) (the reaction was degassed under vacuum). The solution was allowed to stir under an H_2 atmosphere for 22 hr. The solution was filtered through wet celite and the celite washed with EtOH. The filtrate was concentrated under vacuum to yield 4-(6-Amino-5-hydroxy-pyridin-3-yl)-benzoic acid methyl ester (2.3 g, 9.3 mmol, 31%). ^1H NMR (MeOD, 300 MHz) δ 3.90 (s, 3H), 7.21 (d, 1H, *J*, 1.9 Hz), 7.62 (d, 2H, *J*, 8.5 Hz), 7.76 (d, 1H, *J*, 1.9 Hz), 8.04(d, 2H, *J*, 8.5 Hz).

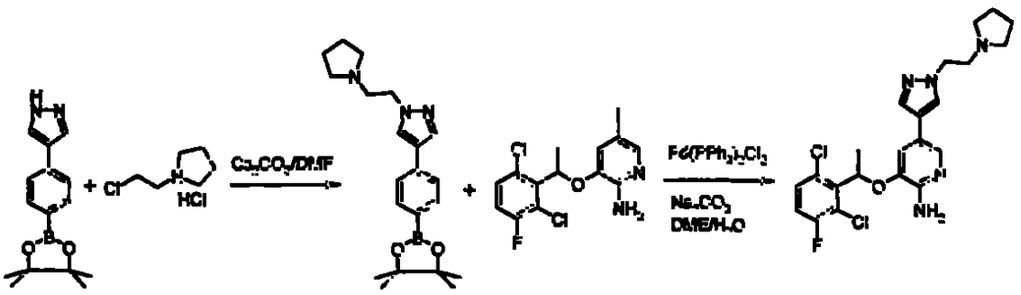
4. To a stirring solution of 4-(6-amino-5-hydroxy-pyridin-3-yl)-benzoic acid methyl ester (2.3 g, 9.3 mmol) in CH_2Cl_2 (180 mL) was added N,N-diisopropylethylamine (3.2 mL, 0.019 mol), 4-methylbenzenesulfonyl chloride (2.66 g, 0.014 mol), and PS-DMAP (catalytic amount). The reaction was stirred at ambient temperature for 6 hr then filtered to remove the resin. The resin was washed with CH_2Cl_2 (3 x 20 mL), and the combined fractions were washed with 10% citric acid (100 mL), saturated NaCl (100 mL), dried (Na_2SO_4) and filtered and concentrated in vacuo. The resulting crude material was purified by column chromatography (silica gel, 100% CH_2Cl_2 to 95:5 CH_2Cl_2:MeOH) and the fractions containing the desired product were combined and concentrated in vacuo to yield 4-[6-Amino-5-(toluene-4-sulfonyloxy)-pyridin-3-yl]-benzoic acid methyl ester (3.3 g, 8.2 mmol, 88%). ^1H NMR ($CDCl_3$, 300 MHz) δ 2.47 (s, 3H), 3.93 (s, 3H), 4.81-4.88 (brs, 2H), 7.36-7.44 (m, 5H), 7.81 (d, 2H, *J*, 8.3 Hz), 8.05 (d, 2H, *J*, 8.4 Hz), 8.19-8.27 (brs, 1H).

5. To a stirred solution of 1-(3-fluoro-2-trifluoromethyl-phenyl)-ethanol (2.0 g, 9.6 mmol) in anhydrous DMF (500 mL) at 0°C under a N_2 atmosphere was added NaH (0.38 g, 9.6 mmol). The reaction was allowed to stir for 0.5 hr. A solution of 4-[6-Amino-5-(toluene-4-sulfonyloxy)-pyridin-3-yl]-benzoic acid methyl ester (3.8 g, 9.6 mmol) in anhydrous DMF (30 mL) was added to the reaction mixture which was allowed to come to ambient temperature slowly and stirred for 21 hr at this temperature. The reaction was diluted with EtOAc (500 mL) and H_2O (100 mL). The organic layer was separated off and the aqueous was further extracted with EtOAc (1 x 200 mL). The organic layers were combined and washed with brine (1 x 100 mL), dried with Na_2SO_4 and concentrated to dryness under vacuum. The crude mixture was purified by column chromatography (silica gel, 40:60 to 70:30 EtOAc:hexanes) and the fractions containing product were combined and concentrated in vacuo to yield 4-(6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl)-benzoic acid methyl ester (1.4 g, 3.2 mmol, 34%). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.73 (d, 3H, *J*, 6.2 Hz), 3.91 (s, 3H), 4.87-4.64 (brs, 2H), 5.81 (q, 1H, *J*, 6.1, 6.3 Hz), 6.92 (d, 1H, *J*, 1.8 Hz), 7.38 (d, 2H, *J*, 8.5 Hz), 7.48-7.66 (m, 3H), 7.93 (d, 1H, *J*, 1.8 Hz), 8.02 (d, 2H, *J*, 8.5 Hz).

8. To a stirred solution of 4-[6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid methyl ester (1.4 g, 3.2 mmol) in warm IPA (72 mL) was added H_2O (38 mL) containing LiOH (0.68 g, 16.2 mmol). The reaction was heated to reflux for 3.5 hr. The reaction was neutralized and diluted with EtOAc (200 mL) and extracted upon cooling. The organic layer was washed with brine (50 mL), dried over Na_2SO_4 and concentrated under vacuum to yield 4-[6-Amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid (1.2 g, 2.8 mmol, 88%). ^{1}H NMR (MeOD, 300 MHz) δ 1.75 (d, 3H, J, 6.2 Hz), 4.88-4.93 (m, 1H), 7.01 (d, 1H, J, 1.8 Hz), 7.39 (d, 2H, J, 8.3 Hz), 7.52-7.67 (m, 3H), 7.80 (d, 1H, J, 1.8 Hz), 7.97 (d, 2H, J, 8.3 Hz).

7. Preparation of amide compounds: A stirring solution of 4-[6-Amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid (50 mg, 0.12 mmol), EDC (27.0 mg, 0.13 mmol) and HOBt (18.0 mg, 0.13 mmol) in DMF (2 mL) was added to a two dram vial containing NHR_1R_2 (0.12 mmol). The reaction was stirred at room temperature for 18 hr. The reaction was then diluted with CH_2Cl_2 (3 mL) and partitioned with H_2O. The organic was separated washed with saturated NaCl (1 x 2 mL) and saturated $NaHCO_3$ (1 x 2 mL). The organic was concentrated to dryness under vacuum. The material was purified using column chromatography (silica gel, 99:1 to 95:5 CH_2Cl_2/MeOH). The fractions containing product were concentrated under vacuum to yield amide compounds.

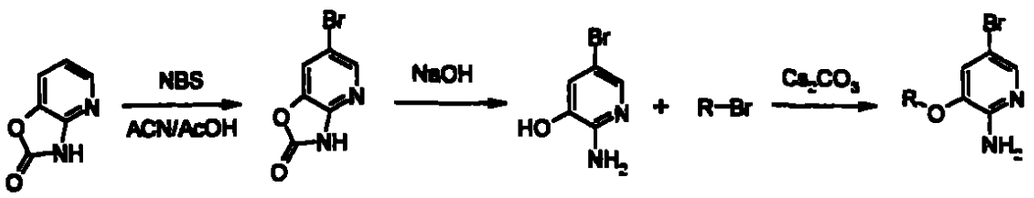
General Procedure 14:



1: To a mixture of 1-(2-chloroethyl)pyrrolidine hydrochloride (200 mg, 1.18 mmol) and 4-[4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-pyrazole (229 mg, 1.19 mmol) in DMF (5 mL) was added Cs_2CO_3. The mixture was stirred at room temperature overnight. Water (10 mL) was then added to the mixture. The product was extracted with EtOAc (3 x 10 mL). The combined extracts were then washed with brine (5 x 10 mL) to remove the DMF, then dried over Na_2SO_4, and concentrated (142 mg, 41% yield).

2: To a mixture of 3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-iodo-pyridin-2-ylamine (200 mg, 0.468 mmol), pinacol boronic ester (1.2 eq), Na_2CO_3 (149 mg, 1.41 mmol) in water (1.25 mL), and dimethyl ethyl glycol (3.75 mL, 0.1M) was added $Pd(PPh_3)_2Cl_2$ (16 mg, 0.020 mmol) in a microwave reaction vessel. The system was degassed and charged with nitrogen. The mixture was stirred at 160°C in a microwave apparatus for 15 minutes. The mixture was cooled to room temperature followed by the addition of water (10 mL). The product was extracted with EtOAc (3 x 20 mL), dried over Na_2SO_4, and concentrated. The crude product was purified by reverse phase HPLC with 0.1% TFA in water and acetonitrile.

General Procedure 15:

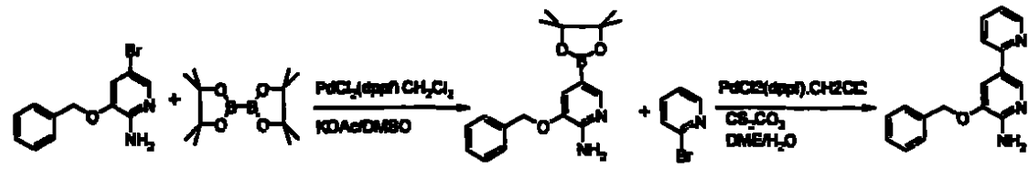


1: To a solution of 3*H*-oxazolo[4,5-*b*]pyridin-2-one (13.6 g, 100 mmol) in acetonitrile (600 mL) and acetic acid (120 mL) was added N-bromosuccinimide (21.4 g, 120 mmol). The mixture was stirred at room temperature for 4 hr and the reaction was quenched with $Na_2S_2O_5$ solution. After evaporation, the residue was partitioned between ethyl acetate and water. The organic layer was washed with 2N NaOH solution, brine, and dried over Na_2SO_4. The crude product was purified on a silica gel column to provide 6-bromo-3*H*-oxazolo[4,5-b]pyridin-2-one (11.5 g, 55% yield).

2: 6-Bromo-3*H*-oxazolo[4,5-b]pyridin-2-one (21.5 g, 100 mmol) was supended in NaOH solution (2N, 250 mL, 500 mmol). The mixture was refluxed overnight and a clear solution was obtained. After cooling to room temperature, the reaction solution was neutralized to pH ~7. A lot of CO_2 was released and also precipitate was observed. The product was filtered, washed with water, and dried under high vacuum to provide 2-amino-5-bromo-pyridin-3-ol as an off-white solid (17.8 g, 96% yield).

3: To a solution of 2-amino-5-bromo-pyridin-3-ol (358 mg, 1.89 mmol) in DMF (8 mL) was added Cs_2CO_3 (620 mg, 1.89 mmol). The mixture was stirred at room temperature under nitrogen for 1 hr. To the reaction mixture was added bromo-compound (0.9 eq) in DMF (5 mL) slowly. The reaction solution was stirred under nitrogen for five hr, and then partitioned between water and ethyl acetate. The organic layer was washed with brine for three times, dried over $MgSO_4$. The crude product was purified on a silica gel column eluting with hexane-ethyl acetate (4:1) to provide the product with 70%-80% yield.

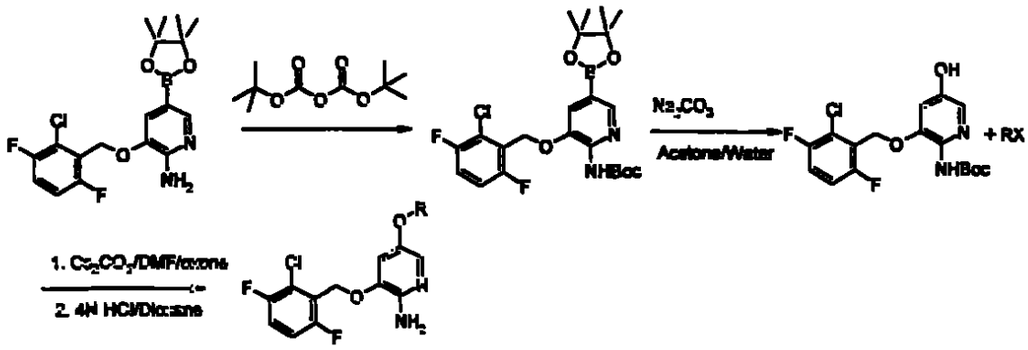
General Procedure 16 using Example I-488:



1. To a solution of 3-benzyloxy-5-bromo-pyridin-2-ylamine (1 g, 3.58 mmol) in dimethylsulfoxide (7 mL) was added sequentially bis(pinacolato)diborane (1.0 g, 3.94 mmol), potassium acetate (1.05 g, 10.7 mmol) [1,1'-bis(diphenylphosphino)ferrocine]dichloropalladium (II), complex with dichloromethane (1:1) (146 mg, 0.18 mmol). The mixture was heated to 80°C for 16 hr and then cooled to room temperature. The reaction mixture was diluted with ethyl acetate (50 mL) and filtered. The filtrate was washed with water (2X50 mL) and dried over magnesium sulfate. Concentration in vacuo yielded the crude boronate as a brown solid (1.13 g, 97%). ^1H NMR ($CDCl_3$) δ 1.32 (s, 12 H), 5.08 (s, 2H), 5.44 (br s, 2H), 7.33-7.42 (m, 6H), 8.03 (s, 1H).

2. An 18 mL reaction vessel was charged with the crude 3-benzyloxy-5-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-pyridin-2-ylamine (161 mg, 0.49 mmol), dimethoxyethane (3 mL) and 2-bromopyridine (117 mg, 0.74 mmol). To this solution was added [1,1'-bis(diphenylphosphino)ferrocine]dichloropalladium (II), complex with dichloromethane (1:1) (20 mg, 0.05 mmol) and a 2 M solution of cesium carbonate in water (0.75 mL, 1.5 mmol). The reactor was warmed to 80°C for 66 hr under a nitrogen atmosphere, then cooled to room temperature. The reaction mixture was partitioned between ethyl acetate (5 mL) and water (5 mL). The organic layer was washed with additional water (5 mL) and diluted with dimethylformamide (5 mL). Polymer-bound sulfonic acid (0.5 g, 2.1 mmol) was added to the organic solution, and the resulting mixture was gently agitated for 2 hr. The resin was filtered and washed with dimethylformamide, methanol and methylene chloride (3X5 mL each solvent). Then the polymer was reacted with 2 M ammonia in methanol for 1 hr. The resin was filtered and washed with additional 2 M ammonia in methanol (2X5 mL), and the combined filtrates were concentrated in vacuo. Purification of the crude product by flash column chromatography yielded 52.2 mg of product as a tan solid (38% yield).

General Procedure 17:

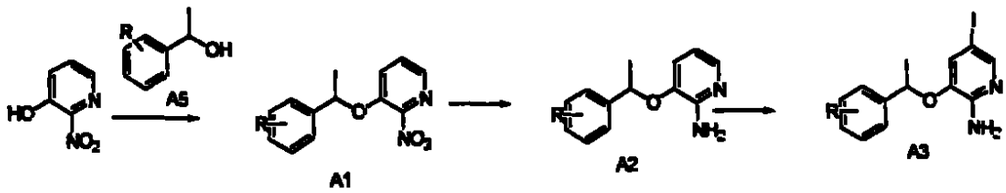


1. To the solution of 3-(2-Chloro-3,6-difluoro-benzyloxy)-5-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-pyridin-2-ylamine (procedure 16) (10.0 g, 24.3 mmol) in *t*-butyl alcohol (50 mL) was added boc anhydride (5.83 g, 26.7 mmol) and reaction stirred at room temperature overnight. Additional boc anhydride (2.25 g, 10.3 mmol) was added and reaction stirred overnight again. Material was concentrated to a viscous black oil and used as-is.

2. The crude boronic ester (24.3 mmol theoretical) in THF (150 mL) was added to a solution of sodium bicarbonate (16.3 g, 194 mmol) in water (150 mL) and acetone (23 mL). The mixture was cooled to 2°C and oxone (13.5 g, 21.9 mmol) added slowly, keeping temperature below 8°C. Upon completion of addition, reaction was stirred fro 5 minutes then quenched with sodium bisulfite (14.2 g) in water (28 mL). Ethyl acetate was added (200 mL) and layers separated. Aqueous layer was neutralized with 6N HCl and extracted with ethyl acetate (2x200 mL). Combined organics were washed with water (250 mL) and brine (250 mL), dried (Na_2SO_4) and concentrated to a crude black oil. Silica gel chromatography (ethyl acetate/hexane) gave the product as a light brown foam (4.78 g, 49.0 %). ^1H NMR ($CDCl_3$) δ 1.48 (s, 9H), 1.74 (d, 3H), 5.75 (q, 1H), 6.61 (d, 1H), 76.89 (dt, 1H), 6.94-7.04 (m, 2H), 7.26(d, 1H), 8.19 (bs, 1H). MS *m/z* 401 $(M+H)^+$.

3. To cesium carbonate in a 2 dram vial was added [3-(2-Chloro-3,6-difluoro-benzyloxy)-5-hydroxy-pyridin-2-yl]-carbamic acid tert-butyl ester (100 mg, 0.25 mmol) in anhydrous DMF (1 mL) followed by benzyl bromide (89.2 µL, 0.75 mmol). The vial was capped and stirred at 90°C overnight. Reaction was filtered through a 5 mL Chem-Elut tube pre-wetted with water (3.5 mL) and eluted with 1:1 ethyl acetate:methylene chloride. After partial concentration, 4N HCl in dioxane (1-2 mL) was added and solution concentrated. Reverse phase chromatography (water:acetonitrile, 0.05% TFA) followed by lyophilization, gave the desired product as an off white amorphous solid (25.3 mg, 20.0 %) and the bis-addition product as a tan amorphous solid (35.2 mg, 23.7 %).

General Procedure 18:



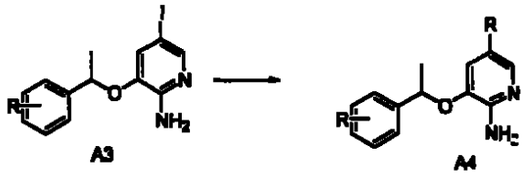
Sodium borohydride (1.5 molar equivalent) was added to solution of ketone (3.89 mmol) in 10 mL of ethanol under a nitrogen atmosphere. The resulting mixture was stirred at room temperature for 12 hr. The mixture was then put in an ice bath and quenched with dilute aqueous HCl. The ethanol was evaporated and EtOAc was added to extract the aqueous solution. The EtOAc layer was dried over Na_2SO_4. The Na_2SO_4 was filtered off and the filtrated was evaporated to give a oil residue, compound A5. The residue was used without further purification.

3-Hydroxy-2-nitropyridine (1.1 molar equivalent) and triphenylphosphine (1.5 molar equivalent) were added to a solution of compound A5 (1.1 mmol) in 10 mL of THF. The reaction mixture was then put in an ice bath and diisopropyl azodicarboxylate (1.5 molar equivalent) was added. The ice bath was removed and the mixture was stirred at room temperature for 12 hr. The solvent was evaporated to give a yellow oil residue. The residue was purified by silica gel chromatography (eluting EtOAc in hexanes) to give compound A1.

2 *M* HCl (0.2 mL) was added to solution of compound A1 (0.97 mmol) in 2 mL of ethanol. The mixture was then put in an ice bath and Fe powder (385 mg) was added slowly. The reaction was heated to 85°C for 1 hr and cooled to room temperature. Celite (0.5 g) was added to stir and the resulting mixture was filtered through a bed of celite and rinsed with ethanol. The filtrated was evaporated to give a brown oil residue, compound A2. The residue was used without further purification.

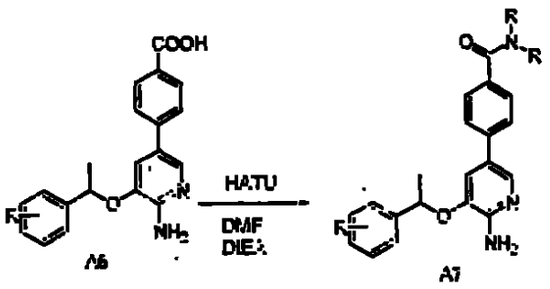
Periodic acid (0.25 molar equivalent), Iodine (0.5 molar equivalent), H_2O (0.5 mL), and concentrate sulfuric acid (0.03 mL) were added to a solution of compound A2 in 3 mL of acetic acid. The reaction mixture was heated to 85°C for 5 hr. The reaction mixture was then cooled in an ice bath and basified with sat. aq. Na_2CO_3 to a pH of 3-4. Ethyl acetate was added to extract the aqueous solution. Dry EtOAc layer over Na_2SO_4. The Na_2SO_4 was filtered off and the filtrated was evaporated to give a brown oil residue. The residue was purified by silica gel chromatography (eluting with EtOAc and hexanes) to give desired product, compound A3.

General Procedure 19:



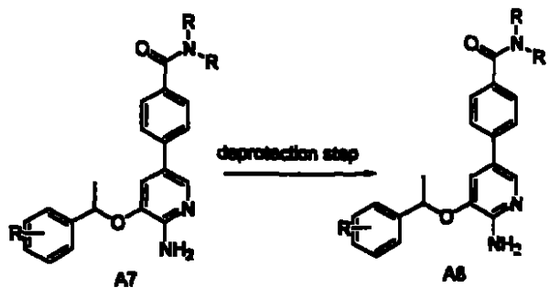
Boronic ester or boronic acid (1.3 molar equivalent) was added to a solution of compound A3 (0.47 mmol) in 5 mL of DME. The mixture was perged with nitrogen several times and then dichlorobis(triphenylphosphino) palladium (II) (0.05 molar equivalent) was added. Sodium carbonate (3 molar equivalent) in 1 mL of H_2O was added to the reaction mixture and the resulting solution was heated to 85°C for 12 hr. Water was added to the reaction mixture to quench the reaction. EtOAc was then added to extract the aqueous solution. Dry EtOAc layer over Na_2SO_4. The Na_2SO_4 was filtered off and the filtrated was evaporated to give a dark brown oil residue. The residue was purified by silica gel chromatography (eluting with CH_3OH, CH_2Cl_2, EtOAc, and hexanes) to give desired product, compound A4.

General Procedure 20:



Compound A6 was prepared using general procedure 19. O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium phosphorus pentafloride (HATU) (1.1 molar equivalent), diisopropylethyl amine (5 molar equivalent) and amine (1.3 molar equivalent) were added to a solution of compound A6 (0.17 mmol) in 3 mL of DMF under a nitrogen atmosphere. The reaction was allowed to stir at room temperature for 12 hr. Saturated $NaHCO_3$ was added to the reaction mixture to quench the reaction. EtOAc was then added to extract the aqueous solution. Dry EtOAc layer over Na_2SO_4. The Na_2SO_4 was filtered off and the filtrate was evaporated to give a brown oil residue. The residue was purified by silica gel chromatography (eluting with EtOAc and hexanes) to give desired amide product, compound A7, as a yellow oil.

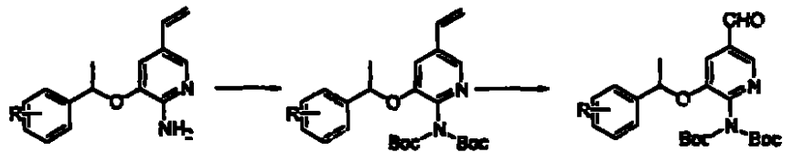
General Procedure 21:



A7 A8

Acid (16 molar equivalent or less) was added to compound A7 (0.13 mmol) at room temperature. The resulting solution was stirred at room temperature or heated to 60°C for 12 hr. The reaction mixture was evaporated and the residue was purified by silica gel chromatography (eluting with CH_3OH, EtOAc and CH_2Cl_2) to give desired amide product, compound A8, as a yellowish to white solid.

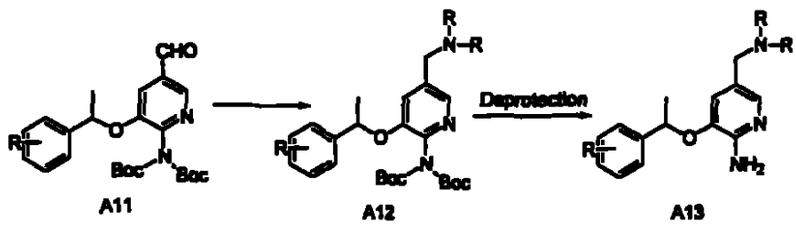
General Procedure 22:



A9 A10 A11

Compound A9 was prepared using general procedure 19. Di-*tert*-butyl dicarbonate (3 molar equivalent) and 4-(dimethylamino)pyridine (0.1 molar equivalent) were added to a solution of compound A9 (3 mmol) in 20 mL of DMF. The reaction mixture was stirred at room temperature for 12 hr. Water was added to the reaction mixture to quench the reaction. EtOAc was then added to extract the aqueous solution. Dry EtOAc layer over Na_2SO_4. The Na_2SO_4 was filtered off and the filtrated was evaporated to give a brown yellow oil residue. The residue was purified by silica gel chromatography (eluting with 25→30 % EtOAc in hexanes) to give desired product, compound A10 as a yellowish oil (87.8% yield). Ozone was bubbled through a solution of compound A10 in 50 mL of CH_2Cl_2 at –78°C and dimethyl sulfide was added to quench the reaction. Saturated sodium chloride was added to the reaction mixture and EtOAc was added to extract the aqueous solution. Combined EtOAc layer was dried over Na_2SO_4. The Na_2SO_4 was filtered off and the filtrated was evaporated to give a yellow oil residue. The residue was purified by silica gel chromatography (eluting with 35→40 % EtOAc in hexanes) to give desired product, compound A11 as a yellowish oil (58.4% yield).

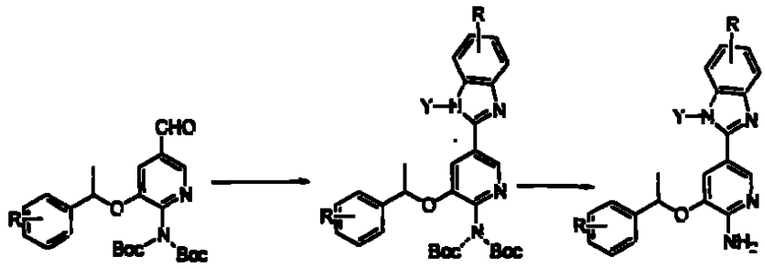
General Procedure 23: Reductive Amination



A11 A12 A13

Amine hydrochloride salt (1.2 molar equivalent), sodium acetate (2 molar equivalent to the amine hydrochloride salt) were added to a solution of compound A11 (0.45 mmol) in 4 mL of CH_3OH under a nitrogen atmosphere. Molecular sieve (0.5 g) was added to the reaction mixture and then sodium cyanoborohydride (2 molar equivalent) was added. The resulting mixture was stirred at room temperature for 12 hr under a nitrogen atmosphere. The reaction mixture was filtered through a bed of celite and the filtrate was evaporated and purified by silica gel chromatography (eluting CH_3OH, EtOAc, and CH_2Cl_2) to give desired product, compound A12 as an oil (52.6% yield). Acid (16 molar equivalent or less) was added to compound A12 (0.17 mmol) at room temperature. The resulting solution was stirred at room temperature or heated to 60°C for 12 hr. The reaction mixture was evaporated and the residue was purified by silica gel chromatography (eluting with CH_3OH, EtOAc and CH_2Cl_2) to give desired product, compound A13.

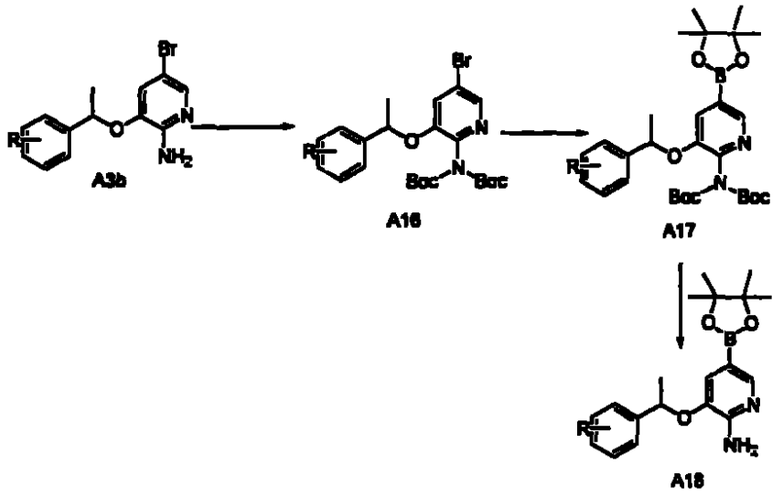
General Procedure 24:



A11 A14 A15

O-phenylidiamine (1.2 molar equivalent) and sodium bisulfite (2.1 molar equivalent) were added to a solution of compound A11 (0.41 mmol) in 5 mL of DMA. The resulting solution was heated to 110°C for 12 hr. Water was added to the reaction mixture to quench the reaction. EtOAc was then added to extract the aqueous solution. Dry EtOAc layer over Na_2SO_4. The Na_2SO_4 was filtered off and the filtrated was evaporated to give a brown yellow oil residue. The residue was purified by silica gel chromatography (eluting with EtOAc in hexanes) to give desired product, compound A14. Acid (16 molar equivalent or less) was added to compound A14 (0.16 mmol) at room temperature. The resulting solution was stirred at room temperature or heated to 60°C for 12 hr. The reaction mixture was evaporated and the residue was purified by silica gel chromatography (eluting with CH_3OH, EtOAc and CH_2Cl_2) to give desired amide product, compound A15.

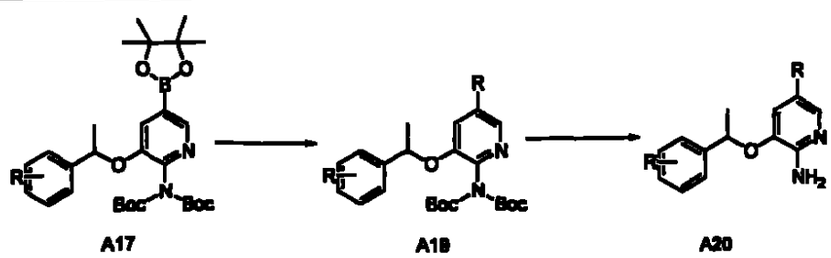
General Procedure 25:



Di-*tert*-butyl dicarbonate (3 molar equivalent), 4-(dimethylamino)pyridine (0.14 molar equivalent) were added to a solution of compound A3b (2 mmol) in 10 mL of DMF. The reaction mixture was stirred at room temperature for 12 hr. Water was added to the reaction mixture to quench the reaction. EtOAc was then added to extract the aqueous solution. Dry EtOAc layer over Na_2SO_4. The Na_2SO_4 was filtered off and the filtrated was evaporated to give a brown yellow oil residue (compound a16). The residue was used without further purification.

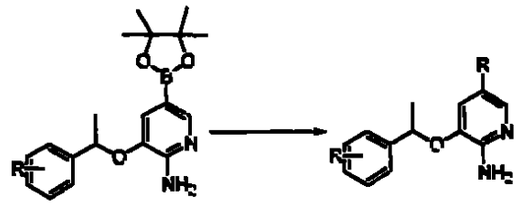
Bis(pinacolato)diboron (1.2 molar equivalent) and potassium acetate (3.4 molar equivalent) were added to a solution of compound a16 in 4 mL of DMSO. The mixture was purged with nitrogen several times and then dichlorobis(triphenylphosphino) palladium (II) (0.05 molar equivalent) was added. The resulting solution was heated to 80°C for 12 hr. Water was added to the reaction mixture to quench the reaction. EtOAc was then added to extract the aqueous solution. Dry EtOAc layer over Na_2SO_4. The Na_2SO_4 was filtered off and the filtrated was evaporated to give a dark brown oil residue. The residue was purified by silica gel chromatography (eluting with 30% EtOAc in hexanes) to give desired product, compound A17 (76% yield). HCl (5 molar equivalent) was added to a solution of compound A17 (0.43 mmol) in 4 mL of CH_2Cl_2. The resulting mixture was heated to 50°C for 12 hr. Saturated $NaHCO_3$ was added to the reaction mixture to neutralize the reaction. EtOAc was then added to extract the aqueous solution. Dry EtOAc layer over Na_2SO_4. The Na_2SO_4 was filtered off and the filtrated was evaporated to give the desired product (compound A18) as a yellow solid (75% yield).

General Procedure 26:



Compound A17 (1.3 molar equivalent) was added to a solution of aryl halide (0.36 mmol) in 3 mL of DME. The mixture was perged with nitrogen several times and then dichlorobis(triphenylphosphino) palladium (II) (0.05 molar equivalent) was added. Sodium carbonate (3 molar equivalent) in 0.8 mL of H_2O was added to the reaction mixture and the resulting solution was heated to 85°C for 12 hr. Water was added to the reaction mixture to quench the reaction. EtOAc was then added to extract the aqueous solution. Dry EtOAc layer over Na_2SO_4. The Na_2SO_4 was filtered off and the filtrated was evaporated to give a dark brown oil residue. The residue was purified by silica gel chromatography (eluting with EtOAc in hexanes) to give desired product, compound A19 (74.4% yield). HCl (5 molar equivalent) was added to a solution of compound A19 (0.26 mmol) in 10 mL of isopropyl alcohol. The resulting mixture was heated to 50°C for 12 hr. The solvent was evaporated to give the desired product, compound A20.

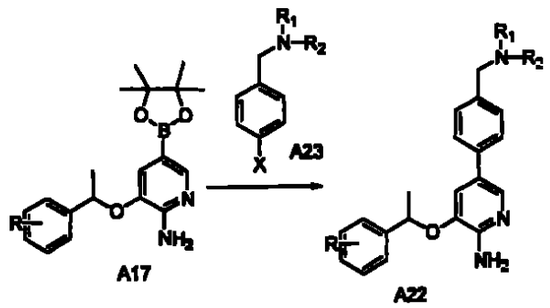
General Procedure 27:



A18 A21

Compound A18 (1.3 molar equivalent) was added to a solution of aryl halide (0.21 mmol) in 3 mL of DME. The mixture was perged with nitrogen several times and then dichlorobis(triphenylphosphino) palladium (II) (0.05 molar equivalent) was added. Sodium carbonate (3 molar equivalent) in 0.6 mL of H_2O was added to the reaction mixture and the resulting solution was heated to 85°C for 12 hr. Water was added to the reaction mixture to quench the reaction. EtOAc was then added to extract the aqueous solution. Dry EtOAc layer over Na_2SO_4. The Na_2SO_4 was filtered off and the filtrated was evaporated to give a dark brown oil residue. The residue was purified by silica gel chromatography (eluting with CH_3OH, CH_2Cl_2, EtOAc, and hexanes) to give desired product, compound A21.

General Procedure 28:



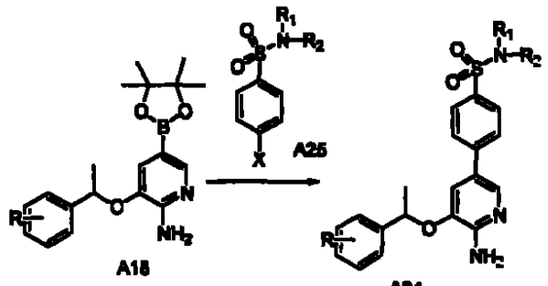
A17 A23 A22

X = I, Br, Cl

Amine (1.5 molar equivalent) and K_2CO_3 (1.5 molar equivalent) were added to a solution of 4-halobenzyl halide (1.0 molar equivalent) in 2 mL of toluene. The resulting mixture was microwaved

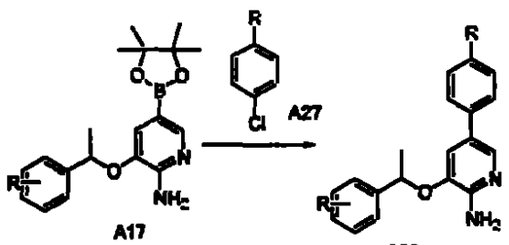
using Smithsynthesizer (150°C, 1 hr). Water was added to the reaction mixture to quench the reaction. EtOAc was then added to extract the aqueous solution. Dry EtOAc layer over Na_2SO_4. The Na_2SO_4 was filtered off and the filtrated was evaporated to give the desired product, compound A23. The residue was used in procedure 11 without further purification to synthesize compound A22.

General Procedure 29:



Amine (1.2 molar equivalent) and diisopropylamine (5 molar equivalent) were added to a solution of 4-bromobenzenesulfonyl chloride (0.77 mmol) in 5 mL of $CHCl_3$ under a nitrogen atmosphere. The resulting mixture was stirred at room temperature for 4 hr. Water was added to the reaction mixture to quench the reaction. EtOAc was then added to extract the aqueous solution. Dry EtOAc layer over Na_2SO_4. The Na_2SO_4 was filtered off and the filtrated was evaporated to give the desired product, compound A25. The residue was used in procedure 11 without further purification to synthesize compound A24.

General Procedure 30:



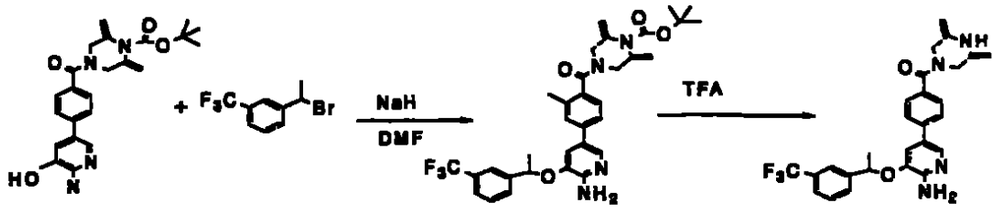
Boronic ester or boronic acid (1.2 molar equivalent) was added to a solution of 1-chloro-4-iodobenzene (0.84 mmol) in 10 mL of ethylene glycol diemthylether (DME) under a nitrogen atmosphere. The mixture was perged with nitrogen several times and then dichlorobis(triphenylphsophino) palladium (II) (0.05 molar equivalent) was added. Sodium carbonate (3 molar equivalent) in 1.8 mL of H_2O was added to the reaction mixture and the resulting solution was heated to 85°C for 12 hr. Water was added to the reaction mixture to quench the reaction. EtOAc was then added to extract the aqueous solution. Dry EtOAc layer over Na_2SO_4. The Na_2SO_4 was filtered off and the filtrated was evaporated to give a dark brown oil residue. The residue was purified by silica gel chromatography (eluting with CH_3OH, CH_2Cl_2, EtOAc, and hexanes) to give desired product, compound A27. Compound A27 was used in procedure 11 to synthesize compound A26.

General Procedure 31 for Chiral Separation of Racemates:

55

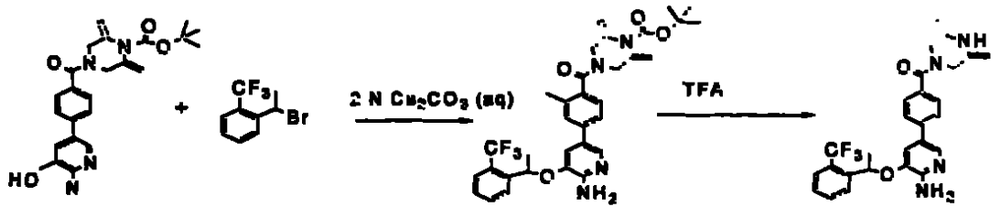
The racemic sample was purified using preparative supercritical fluid chromatoghraphy SFC-MS. The purification conditions were: column- Chiralpak AD-H, 250x21mm, 5 micron, 100A column (Column #:ADH0CJ-C1003); column temperature 35°C; mobile phase 35% methanol (with 0.1% isopropylamine)-modified CO_2; preparative flow rate 52 mL/min; isobaric pressure at 120 bar. The specific chirality of the isomers was not definitively determined.

General Procedure 32: using Example I-617



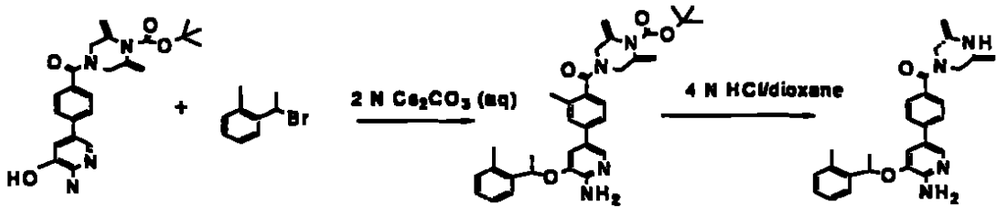
To a mixture of 4-[4-(6-Amino-5-hydroxy-pyridin-3-yl)-benzoyl]-2,6-dimethyl-piperazine-1-carboxylic acid tert-butyl ester (100 mg, 0.23 mmol) and 1-(1-bromo-ethyl)-3-trifluoromethyl-benzene (64 mg, 0.25 mmol) in DMF (2 ml) was added NaH (12 mg, 0.47 mmol) at 0°C. The mixture was stirred overnight. LCMS showed that the reaction was completed, DMF and water were removed. TFA (2 mL) was added to the residue and stirred at room temperature for 3 hr. TFA was removed followed by addition of methanol. The residue was purified by prep-HPLC to afford (4-[6-Amino-5-[1-(3-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(3,5-dimethyl-piperazin-1-yl)-methanone (30 mg, yield 25.7%).

General Procedure 33: using Example I-615



To a mixture of 4-[4-(6-Amino-5-hydroxy-pyridin-3-yl)-benzoyl]-2,6-dimethyl-piperazine-1-carboxylic acid tert-butyl ester (50 mg, 0.12mmol) and 1-(1-bromo-ethyl)-2-trifluoromethyl-benzene (32 mg, 0.12 mmol) in DMF (2 ml) was added 2 M Cs_2CO_3 (0.18 mL, 0.35 mmol), followed by water (0.5 mL), the mixture was stirred overnight then heated at 70°C for 8 hr, LCMS showed that the reaction was completed. The DMF and water were removed. TFA (2 mL was added to the residue and stirred at room temperature for 3 hr. The TFA was removed, followed by addition of methanol. The residue was purified by prep-HPLC to afford (4-[6-amino-5-[1-(2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(3,5-dimethyl-piperazin-1-yl)-methanone (20 mg, yield 34.2%).

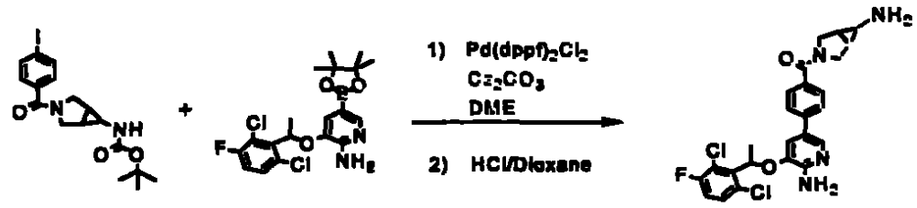
Procedure 34: using Example I-624



In situ

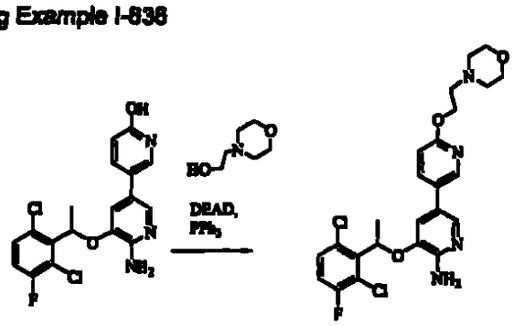
To a mixture of (2R,6S)-4-[4-(6-Amino-5-hydroxy-pyridin-3-yl)-benzoyl]-2,6-dimethyl-piperazine-1-carboxylic acid tert-butyl ester (100 mg, 0.23 mmol) and 1-bromomethyl-2-methyl-benzene (47 mg, 0.25 mmol) in DMF(2 mL) was added 2 M Cs_2CO_3 (0.35 mL, 0.7 mmol) followed by water (0.5 mL). The mixture was stirred at room temperature overnight. LCMS showed the reaction was completed, DMF was removed, followed by addition of 4 N HCl in dioxane (2 mL) and the reaction was stirred at room temperature for 3 hr. The volatiles were removed followed by addition of methanol. This solution was purified by prep-HPLC to afford {4-[6-Amino-5-(2-methyl-benzyloxy)-pyridin-3-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone (47 mg, yield 46.6%).

Procedure 35: using Example I-635



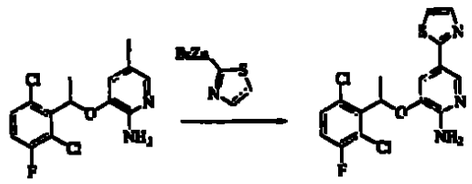
To a mixture of [3-(4-iodo-benzoyl)-3-aza-bicyclo[3.1.0]hex-6-yl]-carbamic acid tert-butyl ester (100 mg, 0.234 mmol) and 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-pyridin-2-ylamine (100 mg, 0.234 mmol) in DME (2 mL) was added $Pd(dppf)_2Cl_2.CH_2Cl_2$ (10 mg, 0.012mmol) and Cs_2CO_3 (351 mg, 0.702 mmol). The mixture was bubbled with nitrogen for 10 min then microwaved at 150°C for 30 min. LCMS checked that the reaction was completed. The crude reaction mixture was diluted with ethyl acetate followed by washings with water and brine. The solution was dried over $MgSO_4$. Purification by prep-HPLC afforded a solid. The solid was stirred with 4 N HCl/dioxane (3 mL) for 3 hr at room temperature. Removal of the volatiles led to a residue that was purified by prep-HPLC to afford (6-amino-3-aza-bicyclo[3.1.0]hex-3-yl)-(4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-methanone (30 mg, yield 28%).

Procedure 36: using Example I-636



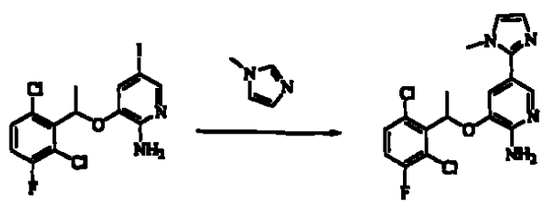
To a mixture of 6'-amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6-ol (78 mg, 0.20 mmol), triphenyphosphine (63 mg, 0.24 mmol) and 2-morpholin-4-yl-ethanol (0.026 mL, 0.22 mmol) was added DEAD (0.034 mL, 0.22 mmol). After stirring overnight more PPh_3 (63 mg, 0.24 mmol) and more DEAD (0.034 mL, 0.22 mmol) were added. After several hours, more alcohol (0.026 mL, 0.22 mmol) was added. After several more hours, more PPh_3 (63 mg, 0.24 mmol) and more DEAD (0.034 mL, 0.22 mmol) were added. After stirring overnight, the mixture was partitioned between dichloromethane and half-saturated brine. The phases were separated and the aqueous phase was extracted with dichloromethane. The combined organic phases were dried over Na_2SO_4 and concentrated by rotary evaporation. The residue was purified by silica gel chromatography using gradient elution of dichloromethane, methanol to afford 5-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-6'-(2-morpholin-4-yl-ethoxy)-[3,3']bipyridinyl-6-ylamine (53 mg, 53%).

Procedure 37: using Example I-650



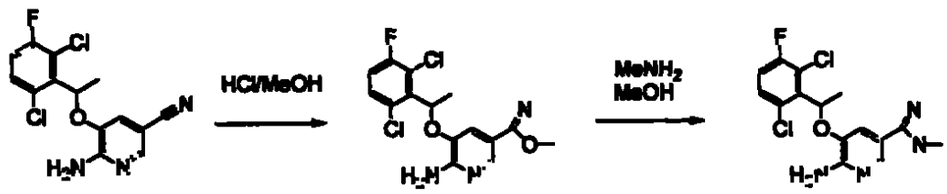
3-(2,6-Dichloro-3-fluoro-benzyloxy)-5-thiazol-2-yl-pyridin-2-ylamine: To a microwave tube equipped with a stir bar was added the Iodo-pyridyl starting material (300 mg, 0.702 mmol), tetrakis(triphenylphosphine) palladium (0) (40 mg, 5 mol%) and tetrahydrofuran (anhydrous, 6 mL). The vial was capped and purged with nitrogen for 5 minutes. 2-Thiazolylzinc bromide (0.5 M in THF, 1.4 mmol, 2.8 mL) was then added via syringe. The vial was heated to 120°C in the microwave for 10 minutes. TLC (1:1 ethyl acetate:methylene chloride) showed a large amount of starting material remaining. Additional 2-thiazolylzinc bromide (0.5 M in THF, 500 µL) was added and the vial was heated to 120°C in the microwave for 20 minutes. TLC (1:1 ethyl acetate:methylene chloride) showed a large amount of starting material still remaining. Additional 2-thiazolylzinc bromide (0.5 M in THF, 500 µL) was added and the vial was heated to 120°C in the microwave for 60 minutes. TLC (1:1 ethyl acetate:methylene chloride) still showed a large amount of starting material still remaining but also had become very messy. The vial contents were poured into a sat. NH_4Cl solution (10 mL) and this solution extracted with ethyl acetate (2 x 30 mL). The combined ethyl acetate layers were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was loaded onto a 10 g prepacked silica gel column and 1:1 ethyl acetate:methylene chloride used to elute the desired product. (40 mg, 15%).

Procedure 38: using Example I-652



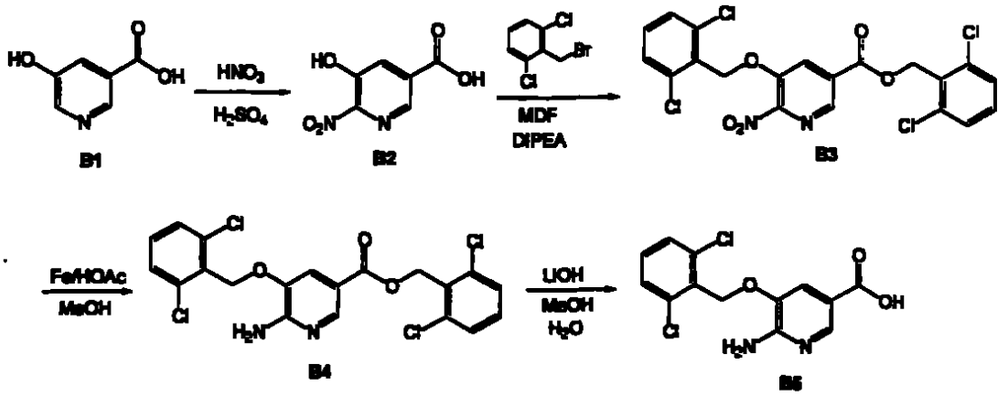
3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(1-methyl-1H-imidazol-2-yl)-pyridin-2-ylamine: N-methyl imidazole (92 mg, 1.1 mmol) was dissolved in tetrahydrofuran (anhydrous, 4 mL) in a 50 mL round bottom flask. The flask was cooled with a dry-ice/acetone bath under nitrogen atmosphere. N-butyl lithium (2.5 M, 582 µL, 1.4 mmol) was added via syringe in 100 µL portions over 5 minutes. The reaction was stirred at –70°C for 30 minutes. Solid zinc chloride (anhydrous, 383 mg, 2.8 mmol) was added and the reaction stirred for 15 minutes. The ice bath was then removed and the reaction allowed to warm to room temperature. Once all of the zinc chloride was in solution and the reaction at room temperature, Iodo scaffold (400 mg, 0.936 mmol) was added in tetrahydrofuran (anhydrous, 4 mL), followed by tetrakis(triphenylphosphine) palladium (0) (108 mg, 10 mol%) and the reaction heated to reflux. The reaction was monitored by LC/MS until all of the starting Iodo scaffold was consumed. The reaction was allowed to cool and then diluted with a sat. NH_4Cl solution (20 mL). This solution was extracted with ethyl acetate (2 x 50 mL). The combined ethyl acetate layers were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was loaded onto a 10 g prepacked silica gel column and 10% methanol:ethyl acetate was used to elute the desired product (25 mg, 7%).

General Procedure 39: using Example I-657



To 6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-nicotinonitrile (400 mg, 1.23 mmol) in 70 mL dry methanol at 0°C was bubbled HCl gas for 3 minutes. Stirred overnight at 3°C. Removed volatiles and washed the solids with diethyl ether to yield quantitatively the imidate. To 200 mg of the imidate in 4 mL methanol at 0°C was added 2N methylamine in THF (837 µL). Let stir at 0°C for about 1 hr then let warm to rt overnight. The volatiles were removed and the residue was chromatographed with 10-20% methanol/dichloromethane to yield 70 mg of product.

General Procedure 40:

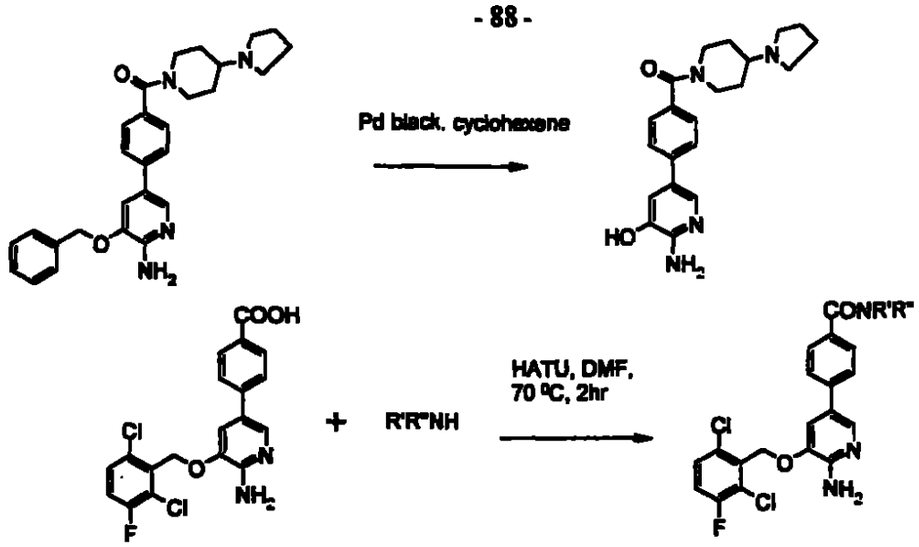


1. 6-Nitro-5-hydroxynicotinic acid (B2): To a solution of 5-hydroxynicotinic acid (B1) (7.0 g, 50 mmol) in concentrated H_2SO_4 was added 9 mL of fuming HNO_3 (90%) (9 mL). The reaction mixture was stirred at 55-60°C in a sealed tube for four days. The mixture was then poured into ice and the pH was adjusted to 3 with 50% NaOH. $MgSO_4$ was added to saturate the aqueous mixture, which was then extracted with isopropyl alcohol (4x45 mL). After the removal of isopropyl alcohol under reduced pressure, 5.93 g (64% yield) of B2 was obtained as a yellow solid. MS (APCI), $(M+H)^+$ 185. ^{1}HNMR (DMSO-d6) δ 8.01 (d, 1H, Ar-H), 8.41(d, 1H, Ar-H).

2. 2,6-Dichlorobenzyl-6-nitro-5-[(2,6-dichlorobenzyl)oxy]nicotinate (B3): 6-nitro-5-hydroxynicotinic acid (B2) (3.4 g, 18.5 mmol), 2,6-dichlorobenzyl bromide (8.88 g, 37 mmol), DIPEA (5.5 g, 42.5 mmol) were dissolved in DMF (25 mL) in a 250 mL round bottomed flask and the reaction was stirred at room temperature for 4.5 hr and then concentrated under reduced pressure. The resulting mixture was poured into ice and the filtered. The solid collected was dried under reduced pressure to give 4.25 g (43% yield) of B3. MS (APCI) $(M+H)^+$ 503. ^{1}HNMR (DMSO-d6) δ 5.47 (s, 2H, $ArCH_2O$), 5.71 (s, 2H, $ArCH_2O$), 7.24-7.43 (m, 6H, Ar-H), 8.26(d, 1H, Ar-H), 8.66(d, 1H, Ar-H).

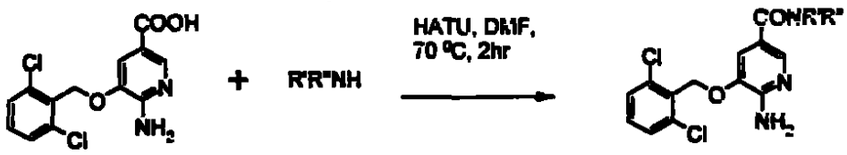
3. 2,6-Dichlorobenzyl-6-amino-5-[(2,6-dichlorobenzyl)oxy]nicotinate (B4): A mixture of 2,6-dichlorobenzyl-6-nitro-5-[(2,6-dichlorobenzyl)oxy]nicotinate (B3) (5.5 g, 10.96 mmol), iron powder (0.92 g, 16.43 mmol), glacial acetic acid (20 mL) and methanol (17mL) was stirred at 85°C for three hr. The reaction mixture was concentrated to near dryness, and ammonium hydroxide (30%) was added to neutralize the mixture. Minimum amount of DMF was added to dissolve the reaction mixture, which was purified by flash column chromatograph (eluent: EtOAc-EtOH, 9:1) to give 4.5 g (87%) of B4 as a pale yellow solid. MS (APCI) $(M+H)^+$ 473.

4. 6-Amino-5-[(2,6-dichlorobenzyl)oxy]nicotinic acid (B5): A mixture of 2,6-dichlorobenzyl-6-amino-5-[(2,6-dichlorobenzyl)oxy]nicotinate (B4) (3.5 g, 7.4 mmol), lithium hydroxide (0.41 g, 17 mmol), water (22 mL) and methanol (30 mL) was stirred and reflux at 85°C for 6 hr. The mixture was concentrated to dryness under reduced pressure. The resulting residue was dissolved in water, extracted with a mixture of Et_2O/hexane (1:1, 4x25 mL), neutralized with 1N HCl to form white precipitation, which was filtered and dried under reduced pressure to provide 1.83 grams (79%) of B5 as a white solid. MS (APCI) $(M+H)^+$ 313. ^{1}HNMR (DMSO-d6) δ 5.26 (s, 2H, $ArCH_2O$), 6.37 (s, 2H, NH_2), 7.43-7.48 (t, 1H, Ar-H), 7.54 (s, 2H, Ar-H), 7.56 (s, 1H, Ar-H), 8.18 (s, 1H, Ar-H).



To an array of 400 µL of 0.2 M solution of different amines in DMF in a 96-well plate was added 400 µL (0.2 M in DMF) of 4-[6-amino-5-(2,6-dichloro-3-fluoro-benzyloxy)-pyridin-3-yl]-benzoic acid, 80 µL of triethylamine (1M in DMF) and 160 µL of HATU (0.5 M in DMF) and the reactions were stirred at 70°C for 2 hr. The solvent was removed using the SpeedVac apparatus and the crude reaction mixtures were redissolved in DMSO and transferred using a liquid handler to a 1mL 96-well plate to give a final theoretical concentration of ~ 10 mM. The reactions were analyzed and positive product identification was made using LC/MS. The mother stock solution was diluted to 50 nM and assayed for percent inhibition of c-MET at 50nM.

General Procedure 41:



To an array of 400 µL of 0.2 M solution of different amines in DMF in a 96-well plate was added 400 µL (0.2 M in DMF) of 6-Amino-5-[(2,6-dichlorobenzyl)oxy]nicotinic acid, 80 µL of triethylamine (1M in DMF) and 160 µL of HATU (0.5 M in DMF) and the reactions were stirred at 70°C for 2 hr. The solvent was removed using the SpeedVac apparatus and the crude reaction mixtures were redissolved in DMSO and transferred using a liquid handler to a 1mL 96-well plate to give a final theoretical concentration of ~ 10 mM. The reactions were analyzed and positive product identification was made using LC/MS. The mother stock solution was diluted to 1 µM and assayed

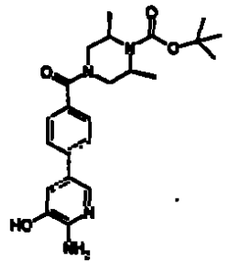
General Procedure 42:

[4-(6-Amino-5-hydroxy-pyridin-3-yl)-phenyl]-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone: To a solution of [4-(6-Amino-5-benzyloxy-pyridin-3-yl)-phenyl]-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone

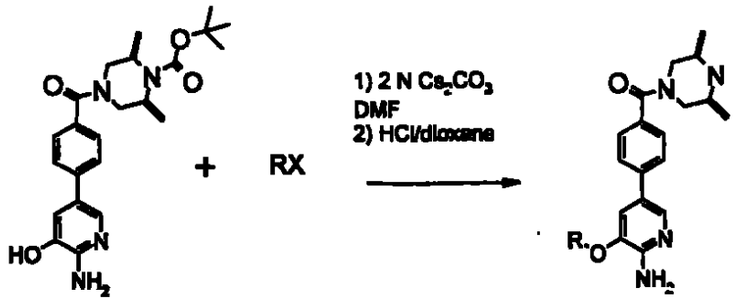
(3.67 g, 8.1 mmol) in 100 ml ethanol was added 25 ml cyclohexne and 367 mg palladium black. Reluxed overnight. The solution was filtered and the volatiles were removed. To the residue was added 60 mL of MeOH, 20 mL cyclohexene and 350 mg Pd black. Refluxed overnight. Filtered and removed volatiles, resuspended in methanol, added 350 mg Pd black and hydrogenated at 1 atm overnight (pressure reactors all busy). Filtered and isolated 3.0 grams of a solid foam. ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 7.82 (d, J=2.02 Hz, 1 H) 7.58 (d, J=8.34 Hz, 2 H) 7.41 (d, J=8.34 Hz, 2 H) 7.12 (d, J=2.02 Hz, 1 H) 5.74 (s, 2 H) 3.33 (s, 5 H) 3.08 (s, 2 H) 1.95 (m, 8 H) 1.49 (s, 2 H). LC/MS(APCI) 367 m/e (M+1).

To an array of 10x75 mm test tubes were added [4-(6-Amino-5-hydroxy-pyridin-3-yl)-phenyl]-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone (0.2 M in DMF, 80 µmol, 1.0 eq.), Cs_2CO_3 (2 M, 160 µmol, 2.0 equiv) and different alkyl halides (0.2 M in DMF, 88 µmol, 1.1 eq.).The reactions were stirred at room temperature overnight. In order to separate the inorganic salts, the resulting suspension was evaporated and DMF (625 µL) was added. After agitation, the mixture was centrifuged to settle the solid residue, and the supernatant was transferred to a new 10x75 mm test tube. The reactions were analyzed and positive product identification was made using LC/MS. The mother stock solution was diluted to 1 µM and assayed.

General Procedure 43:



(2R,6S)-4-[4-(6-Amino-5-hydroxy-pyridin-3-yl)-benzoyl]-2,6-dimethyl-piperazine-1-carboxylic acid tert-butyl ester: See general procedure IG. Yield 83.5%. 1H NMR (400 MHz, DMSO-D6) δppm 7.81 (d, J=2.27 Hz, 1 H) 7.57 (d, J=8.34 Hz, 2 H) 7.41 (d, J=8.34 Hz, 2 H) 7.12 (d, J=2.02 Hz, 1 H) 5.70



(s, 2 H) 4.07 (s, 2 H) 3.31 (s, 3 H) 1.39 (s, 10 H) 1.03 - 1.14 (m, 7 H)

To an array of 10x75 mm test tubes were added [4-(6-Amino-5-hydroxy-pyridin-3-yl)-phenyl]-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone (0.2 M in DMF, 80 µmol, 1.0 eq.), Cs_2CO_3 (2 M, 160 µmol, 2.0

equiv) and different alkyl halides (0.2 M in DMF, 88 µmol, 1.1 eq.).The reactions were stirred at room temperature overnight. In order to separate the inorganic salts, the resulting suspension was evaporated and DMF (625 µL) was added. After stirring, the mixture was centrifuged to settle the solid residue, and the supernatant was transferred to a new 10x75 mm test tube. The solid residues were extracted with more DMF (400 µL) and the extracts were combined with the first organic layer. The DMF was evaporated, and HCl (4 M in dioxane, 2.5 mmol, 31 eq.) was added to the reaction mixture in the receiving test tube. The reaction mixture was stirred at room temperature for 3 hr. The reactions were analyzed and positive product identification was made using LC/MS. The mother stock solution was diluted to 1 µM and assayed.

Example i(a):

1. To a stirred solution of Cs_2CO_3 (11.63 g, 35.69 mmol) in DMF (180 mL) under a N_2 atmosphere containing 3-hydroxy-4-nitro-pyridine (5 g, 35.69 mmol) was added 2,6-dichlorobenzyl bromide (8.58 g, 35.69 mmol). The mixture was stirred for 6 h at ambient temperature. The reaction was then diluted with EtOAc (400 mL) and partitioned with H_2O (100 mL). The aqueous layer was extracted with EtOAc (2 x 50 mL). The organic layers were then combined and washed with H_2O (2 x 50 mL) and brine (1 x 50 mL). The organics were dried over Na_2SO_4, filtered and concentrated to dryness under vacuum to yield 3-(2,6-dichloro-benzyloxy)-2-nitro-pyridine (10.5 g, 98.4%) as a white solid.

2. To a stirred mixture of AcOH (650 mL) and EtOH (500 mL) was suspended 3-(2,6-dichloro-benzyloxy)-2-nitro-pyridine (37.4 g, 0.11 mol) and iron chips (69.4 g, 0.11 mol). The reaction was heated slowly to reflux and allowed to stir for 1 hr. The reaction was cooled to room temperature then filtered through a pad of celite. The resulting filtrate was neutralized with conc. NH_4OH (600 mL) and then extracted with EtOAc (3 x 500 mL). The combined organic extracts were washed with saturated $NaHCO_3$ (2 x 100 mL), H_2O (2 x 100 mL) and brine (1 x 100 mL) then dried (Na_2SO_4), filtered and concentrated to dryness under vacuum to yield 3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine (32.4 g, 0.11 mol, 99%) as a light yellow solid. ^1H NMR (400 MHz, DMSO-d_6) δ 7.56 (m, 3H), 7.46 (dd, 2H), 7.36 (d, 1H), 6.62 (dd, 1H), 6.18 (br s, 2H, NH_2), 5.24 (s, 2H); MS *m/z* 270 [M+1].

3. A stirring solution of 3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine (32.4 g, 0.11 mol) in acetonitrile was cooled to 0°C using an ice bath. To this solution was added *N*-bromosuccinimide (19.5 g, 0.11 mol) portionwise. The reaction was stirred at 0°C for 15 min. The reaction was concentrated to dryness under vacuum. The resulting dark oil was dissolved in EtOAc (500 mL) and partitioned with H_2O (250 mL). The organic was then washed with sat'd $NaHCO_3$ (2 x 200 mL) and brine (1 x 200 mL). Activated charcoal was added to the organic layer and warmed to reflux. The solution was then cooled to room temperature and filtered through a pad of celite. The organic was then concentrated to dryness under vacuum to one third the original volume. The solids were then filtered off to yield 5-bromo-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine (22.0 g, 0.07 mol, 64%) as a tan solid. The remaining filtrate was concentrated under vacuum to yield crude 5-bromo-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine (12.1g, 0.04 mol, 35%) as a brown solid.

Example I(b): 3-Benzyloxy-5-bromo-pyridin-2-ylamine was prepared following procedure 1 from 3-benzyloxy-pyridin-2-ylamine as a tan solid in 65% yield.

Example I(c): 5-Bromo-3-(2,6-difluoro-benzyloxy)-pyridin-2-ylamine was prepared following procedure 1. 3-(2,6-difluoro-benzyloxy)-2-nitro-pyridine was prepared in 99% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.14 (m, 2H), 7.79 (dd, 1H), 7.52 (m, 1H), 7.16 (m, 2H), 5.37 (s, 2H); MS *m/z* 266 [M+]. 3-(2,6-Difluoro-benzyloxy)-pyridin-2-ylamine was prepared in 100% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.88 (s, 2H), 7.64 (dd, 1H), 7.57 (m, 2H), 6.84 (dd, 1H), 5.24 (s, 2H); MS *m/z* 237 [M+1]. 5-Bromo-3-(2,6-difluoro-benzyloxy)-pyridin-2-ylamine was prepared in 91% yield.

Example I(d): 5-Bromo-3-(2-bromo-benzyloxy)-pyridin-2-ylamine was prepared following procedure 1. 3-(2-bromo-benzyloxy)-2-nitro-pyridine intermediate was prepared in 99% yield as a white solid. 3-(2-bromo-benzyloxy)-pyridin-2-ylamine was prepared in 100% yield as a solid. 5-Bromo-3-(2-bromo-benzyloxy)-pyridin-2-ylamine was obtained in 37% yield as a tan solid.

Example I(e): 5-Bromo-3-(2-chloro-6-fluoro-benzyloxy)-pyridin-2-ylamine was prepared following procedure 1. 3-(2-chloro-6-fluoro-benzyloxy)-2-nitro-pyridine was prepared in 90% yield as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.15 (m, 2H), 7.80 (m, 1H), 7.50 (m, 1H), 7.40 (m, 1H), 7.30 (m, 1H), 5.39 (s, 2H). 3-(2-chloro-6-fluoro-benzyloxy)-pyridin-2-ylamine was prepared in 68% yield as a tan solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.70-7.15 (m, 5H), 6.45 (m, 1H), 5.45 (br s, 2H), 5.06 (s, 2H). 5-Bromo-3-(2-chloro-6-fluoro-benzyloxy)-pyridin-2-ylamine was prepared in 81% yield.

Example I(f): 5-Bromo-3-(2-chloro-4-fluoro-benzyloxy)-pyridin-2-ylamine was prepared following procedure 1. 3-(2-chloro-4-fluoro-benzyloxy)-2-nitro-pyridine was prepared in 91% yield as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.08 (m, 2H), 7.75 (m, 1H), 7.63 (m, 1H), 7.55 (m, 1H), 7.25 (m, 1H), 5.45 (s, 2H). 3-(2-chloro-4-fluoro-benzyloxy)-pyridin-2-ylamine was prepared in 100% yield as a tan solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.70 (m, 2H), 7.47 (m, 1H), 7.20 (m, 1H), 7.08 (m, 1H), 6.45 (m, 1H), 5.62 (br s, 2H), 5.08 (s, 2H). 5-Bromo-3-(2-chloro-4-fluoro-benzyloxy)-pyridin-2-ylamine was prepared in 63% yield.

Example I(g): 5-Bromo-3-(2,4-dichloro-benzyloxy)-pyridin-2-ylamine was prepared following procedure 1. 3-(2,4-Dichloro-benzyloxy)-2-nitro-pyridine was prepared in 96% yield as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.05-7.50 (m, 6H), 5.39 (s, 2H); MS *(m/z)* 299 (M+1). 3-(2,4-Dichloro-benzyloxy)-pyridin-2-ylamine was prepared in 98% yield as a tan solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.65-6.25 (m, 6H), 5.85 (br s, 2H), 5.06 (s, 2H). 5-Bromo-3-(2,4-dichloro-benzyloxy)-pyridin-2-ylamine was prepared in 65% yield.

Example I(h): 2-(2-Amino-5-bromo-pyridin-3-yloxymethyl)-benzonitrile was prepared following procedure 1. 2-(2-Nitro-pyridin-3-yloxymethyl)-benzonitrile was prepared in 91% yield as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.15-7.55 (m, 1H), 5.50 (s, 2H). 2-(2-Amino-pyridin-3-yloxymethyl)-benzonitrile was prepared in 86% yield as a tan solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.95-6.45 (m, 7H), 5.65 (br s, 2H), 5.20 (s, 2H). 2-(2-Amino-5-bromo-pyridin-3-yloxymethyl)-benzonitrile was prepared in 77% yield.

Example I(i): 5-Bromo-3-(2-trifluoromethyl-benzyloxy)-pyridin-2-ylamine was prepared following procedure 1. 3-(2-trifluoromethyl-benzyloxy)-2-nitro-pyridine was prepared in 92% yield as an off-white

solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.05-7.58 (m, 7H), 5.45 (s, 2H). 3-(2-trifluoromethyl-benzyloxy)-pyridin-2-ylamine was prepared in 80% yield as a tan solid. 5-Bromo-3-(2-chloro-4-fluoro-benzyloxy)-pyridin-2-ylamine was prepared in 43% yield as a solid.

Example I(j): 5-Bromo-3-(4-*tert*-butyl-benzyloxy)-pyridin-2-ylamine was prepared following procedure 1. 3-(4-*tert*-butyl-benzyloxy)-2-nitro-pyridine was prepared in 80% yield as an oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10-7.30 (m, 7H), 5.30 (s, 2H), 1.25 (s, 9H). 3-(4-*tert*-Butyl-benzyloxy)-pyridin-2-ylamine was prepared in 100% yield as a tan solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.45-6.25 (m, 7H), 5.58 (br s, 2H), 5.05(s, 2H), 1.25 (s, 9H). 5-Bromo-3-(4-*tert*-butyl-benzyloxy)-pyridin-2-ylamine was prepared in 55% yield as a solid.

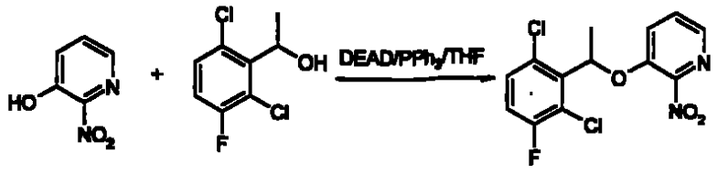
Example I(k): 5-Bromo-3-(2-chloro-benzyloxy)-pyridin-2-ylamine was prepared following procedure 1. 3-(2-Chloro-benzyloxy)-2-nitro-pyridine was prepared in 89% yield as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10-7.40 (m, 7H), 5.40 (s, 2H). 3-(2-Chloro-benzyloxy)-pyridin-2-ylamine was prepared in 100% yield as a tan solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.65-6.45 (m, 7H), 5.62 (br s, 2H), 5.10(s, 2H). 5-Bromo-3-(2-chloro-benzyloxy)-pyridin-2-ylamine was prepared in 22% yield as a solid.

Example I(l): 5-Bromo-3-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-2-ylamine was prepared following procedure 1. 3-(2-chloro-3,6-difluoro-benzyloxy)-2-nitro-pyridine intermediate was prepared in 99% yield as an off white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ5.31 (s, 2H), 7.02-7.09 (dt, 1H, *J*, 4, 8), 7.17-7.23 (dt, 1H, *J*, 4.5, 8.4), 7.54-7.58 (dd, 1H, *J*, 4.5, 8.4), 7.71-7.68 (dd, 1H, *J*,1.21, 8.4), 8.14-8.16 (dd, 1H, *J*, 1.23, 4.5). 3-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-2-ylamine was prepared in 100% yield as a light yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.6-4.8 (brs, 2H), 5.2 (s, 2H), 7.0-7.06 (dt, 1H, *J*, 4.1, 8.0), 7.09-7.12 (dd, 1H, *J*, 1.0, 7.8), 7.15-7.22 (dt, 1H, *J*, 4.8, 8.0), 7.69-7.71 (dd, 1H, *J*, 1.2, 5.1). 5-Bromo-3-(2-chloro3,6-difluoro-benzyloxy)-pyridin-2-ylamine was obtained in 64% yield as a tan solid.

Example I(m): 5-Bromo-3-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-2-ylamine was prepared following procedure 1 starting from 3-hydroxy-4-nitro-pyridine and 1-bromomethyl-3-fluoro-2-trifluoromethyl-benzene.

Example I(n):

1. 2,6-Dichloro-3-fluoroacetophenone (15 g, 0.072 mol) was stirred in THF (150 mL, 0.5M) at 0°C using an ice bath for 10 min. Lithium aluminum hydride (2.75 g, 0.072mol) was slowly added. The reaction was stirred at ambient temperature for 3 hr. The reaction was cooled in ice bath, and water (3 mL) was added drop wisely followed by adding 15% NaOH (3 mL) slowly. The mixture was stirred at ambient temperature for 30 min. 15% NaOH (9 mL), $MgSO_4$ were added and the mixture filtered to remove solids. The solids were washed with THF (50 mL) and the filtrate was concentrated to give 1-(2,6-Dichloro-3-fluoro-phenyl)-ethanol (14.8 gm, 95% yield) as a yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.45 (d, 3H), 5.42 (m, 2H), 7.32 (m, 1H), 7.42 (m, 1H).



2. To a stirred solution of triphenyl phosphine (8.2 g, 0.03 mol) and DEAD (13.65 mL of a 40% solution in toluene) in THF (200 mL) at 0°C was added a solution of 1-(2,6-dichloro-3-fluoro-phenyl)-ethanol (4.55 g, 0.021 mol) and 3-hydroxy-nitropyridine (3.35 g, 0.023 mol) in THF (200 mL). The resulting bright orange solution was stirred under a nitrogen atmosphere at ambient temperature for 4 hours at which point all starting materials had been consumed. The solvent was removed, and the crude material was dry loaded onto silica gel, and eluted with ethyl acetate-hexanes (20:80) to yield 3-(2,6-dichloro-3-fluoro-benzyloxy)-2-nitro-pyridine (6.21 g, 0.021 mol, 98%) as a pink solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ1.8-1.85 (d, 3H), 6.0-6.15 (q, 1H), 7.0-7.1 (t, 1H), 7.2-7.21 (d, 1H), 7.25-7.5 (m, 2H), 8.0-8.05 (d, 1H).

3. 3-(2,6-dichloro-3-fluoro-benzyloxy)-pyridin-2-ylamine was prepared following procedure 1. To a stirred mixture of AcOH (650 mL) and EtOH (500 mL) was suspended 3-(2,6-dichloro-3-fluoro-benzyloxy)-2-nitro-pyridine (9.43 g, 0.028 mol) and iron chips (15.7 g, 0.28 mol). The reaction was heated slowly to reflux and allowed to stir for 1 hr. The reaction was cooled to room temperature then diethyl ether (500 mL) and water (500 mL) was added. The solution was carefully neutralized by the addition of sodium carbonate. The combined organic extracts were washed with sat'd $NaHCO_3$ (2 x 100 mL), H_2O (2 x 100 mL) and brine (1 x 100 mL) then dried (Na_2SO_4), filtered and concentrated to dryness under vacuum to yield 3-(2,6-dichloro-3-fluoro-benzyloxy)-pyridin-2-ylamine (9.04 g, 0.027 mol, 99%) as a light pink solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ1.8-1.85 (d, 3H), 4.9-5.2 (brs, 2H), 5.7-5.84 (q, 1H), 7.0-7.1 (m, 1H), 7.2-7.3 (m, 1H), 7.6-7.7 (m, 1H).

4. 5-bromo-3-(2,6-dichloro-3-fluoro-benzyloxy)-pyridin-2-ylamine was prepared following procedure 1. A stirring solution of 3-(2,6-dichloro-3-fluoro-benzyloxy)-pyridin-2-ylamine (9.07 g, 0.03 mol) in acetonitrile was cooled to 0°C using an ice bath. To this solution was added NBS (5.33 g, 0.03 mol) portionwise. The reaction was stirred at 0°C for 15 min. The reaction was concentrated to dryness under vacuum. The resulting dark oil was dissolved in EtOAc (500 mL), and purified via silica gel chromatography. The solvents were then removed in vacuo to yield 5-bromo-3-(2,6-dichloro-3-fluoro-benzyloxy)-pyridin-2-ylamine (5.8 g, 0.015 mol, 51%) as a white crystalline solid.

Example I(o):



1. 2-Chloro-3,6-difluorobenzaldehyde (1.0 molar equivalent) was dissolved in THF (0.2M) and stirred at 0°C for 5 min. The corresponding methylmagnesium chloride solution (1.1 molar equivalent) was added .The reaction was warmed up gradually to ambient temperature and stirred for 2 hr. Methanol, and 1N HCl was added to the mixture and diluted with ethyl acetate. The mixture was washed

with water, brine, dried over $MgSO_4$, filtered, and concentrated to give 1-(2-chloro-3,6-difluoro-phenyl)-ethanol as oil. ^1H NMR (400 MHz, DMSO-d6) δ 1.42 (d, 3H), 5.21 (m, 1H), 5.42 (m, 1H), 7.09 (m, 1H), 7.18 (m, 1H).

2. 5-bromo-3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-2-ylamine was prepared following the same procedure as Example I(n) starting from 1-(2-chloro-3,6-difluoro-phenyl)-ethanol and 3-hydroxy-nitropyridine.

Example II(a): To an ice cooled solution of (2,6-dichloro-phenyl)-methanol (5 g, 28.2 mmol) in anhydrous tetrahydrofuran (200 mL) was added sodium hydride (1.13 g, 28.2 mmol, 60% disp.) slowly under nitrogen atmosphere. After stirring for 30 minutes, 3,5-dibromo-pyrazin-2-ylamine (7.08 g, 28.2 mmol) in anhydrous tetrahydrofuran (50 mL) was added via an addition funnel. Once the addition was complete the ice bath was removed and the reaction was refluxed under nitrogen and monitored by reversed phase HPLC. After 18 hr HPLC showed that the majority of the starting 3,5-dibromo-pyrazin-2-ylamine had been consumed and the reaction was allowed to cool to room temperature. The reaction mixture was concentrated in vacuum until 50 mL remained. The mixture was diluted with ethyl acetate (200 mL) and extracted with 50% brine (2 x 200 mL). The organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuum. The crude product was purified using a silica gel column eluting with 1:1 ethyl acetate/dichloromethane to yield 5-bromo-3-(2,6-dichloro-benzyloxy)-pyrazin-2-ylamine as a white solid (8.17 g, 83% yield).

Example II(b): 5-Bromo-3-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-ylamine was prepared following procedure 2 from (2-chloro-3,6-difluoro-phenyl)-methanol and 3,5-dibromo-pyrazin-2-ylamine.

Example II(c):

1. 2-Chloro-3, 6-difluorobenzaldehyde (1.0 molar equivalent) was dissolved in THF (0.2M) and stirred at 0°C for 5 min. The corresponding methylmagnesium chloride solution (1.1 molar equivalent) was added .The reaction was warmed up gradually to ambient temperature and stirred for 2 hr. Methanol and 1N HCl were added to the mixture and diluted with ethyl acetate. The mixture was washed with water, brine, dried over $MgSO_4$, filtered, and concentrated to give 1-(2-chloro-3,6-difluoro-phenyl)-ethanol as oil. ^1H NMR (400 MHz, DMSO-d_6) δ 1.42 (d, 3H), 5.21 (m, 1H), 5.42 (m, 1H), 7.09 (m, 1H), 7.18 (m, 1H).

2. 5-bromo-3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-ylamine was prepared following procedure 2 from 1-(2-chloro-3,6-difluoro-phenyl)-ethanol and 3,5-dibromo-pyrazin-2-ylamine.

Example II(d):

1. 1-(2-Chloro-3,6-difluoro-phenyl)-2-methyl-propan-1-ol was prepared following the procedure of Example II(c) using isopropylmagnesium chloride. ^1H NMR (400 MHz, DMSO-d_6) δ 0.83 (d, 3H), 1.06 (d, 3H), 2.19 (m, 1H), 4.59 (m, 1H), 5.54 (d, 1H), 7.21 (m, 1H), 7.36 (m, 1H).

2. 5-bromo-3-[1-(2-chloro-3,6-difluoro-phenyl)-2-methyl-propoxy]-pyrazin-2-ylamine was prepared following procedure 2 from 1-(2-chloro-3,6-difluoro-phenyl)-2-methyl-propan-1-ol and 3,5-dibromo-pyrazin-2-ylamine.

Example II(e):

1. 2,6-Dichloro-3-fluoroacetophenone (15 g, 0.072 mol) was stirred in THF (150 mL, 0.5M) at 0°C using an ice bath for 10 min. Lithium aluminum hydride (from Aldrich, 2.75 g, 0.072mol) was slowly added. The reaction was stirred at ambient temperature for 3 h. The reaction was cooled in ice bath, and water (3 mL) was added drop wisely followed by adding 15% NaOH (3 mL) slowly. The mixture was stirred at ambient temperature for 30 min. 15% NaOH (9 mL), $MgSO_4$ were added and the mixture filtered to remove solids. The solids were washed with THF (50 mL) and the filtrate was concentrated to give 1-(2,6-Dichloro-3-fluoro-phenyl)-ethanol (14.8 gm, 95% yield) as a yellow oil. ^1H NMR (400 MHz, DMSO-d_6) δ 1.45 (d, 3H), 5.42 (m, 2H), 7.32 (m, 1H), 7.42 (m, 1H).

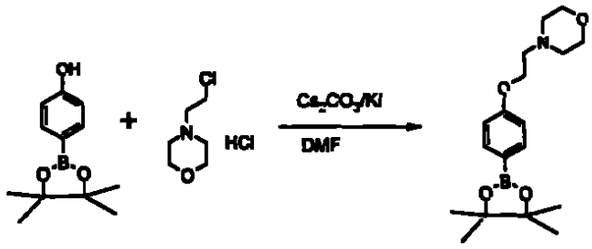
2. 5-Bromo-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-ylamine was prepared following procedure 2 from 1-(2,6-dichloro-3-fluoro-phenyl)-ethanol and 3,5-dibromo-pyrazin-2-ylamine.

Example II(f): 5-Bromo-3-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-ylamine was prepared following procedure 2 from (3-fluoro-2-trifluoromethyl-phenyl)-methanol and 3,5-dibromo-pyrazin-2-ylamine.

Example I-1: A mixture of 5-bromo-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine (example I(a), 100 mg, 0.29 mmol), 4-(4,4,5,5-tetramethyl-1,3-2-dioxaborolan-2-yl) phenol (65 mg, 0.35 mmol), bis(triphenylphosphine) palladium(II) chloride (6 mg, 0.009 mmol) and sodium carbonate (91 mg, 0.87 mmol) in ethylene glycol dimethyl ether (10 mL) and water (0.5 mL) was heated to reflux under nitrogen for 18 hours. The reaction was cooled to ambient temperature and diluted with ethyl acetate. The mixture was washed with water, brine, dried over Na_2SO_4, and purified on silica column to afford 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenol as light pine crystals (89 mg, 85% yield).

Example I-2:

1. To a mixture of 4-(4,4,5,5-tetramethyl-1,3-2-dioxaborolan-2-yl) phenol (5.00 g, 22.72 mmol) and Cs_2CO_3 (16.29 g, 49.98 mmol) in DMF (100 mL) were added 4-(2-chloroethyl)morpholine hydrochloride (4.65 g, 24.99 mmol) and KI (0.2 g, 0.6 mmol). The mixture was stirred at 65°C oil bath

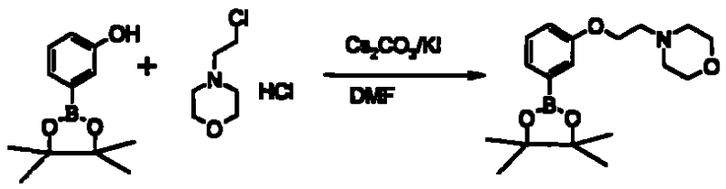


for overnight and then cooled to ambient temperature. The reaction mixture was diluted with ethyl acetate (600 mL), and partitioned with water. The water layer was extracted with ethyl acetate (2X50 mL). The combined ethyl acetate solution was washed with brine (5X100 mL), dried over Na_2SO_4, filtered, condensed, and dried in high vacuum to provide 4-[2-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-ethyl)-morpholine (6.8 g, 90% yield) as an off-white solid. ^1H NMR (400 MHz, DMSO-d_6) δ 7.55 (d, 2H), 6.90 (d, 2H), 4.07 (t, 2H), 3.54 (m, 4H), 2.65 (t, 2H), 2.43 (m, 4H).

2. 3-(2,6-Dichloro-benzyloxy)-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine was prepared from 5-bromo-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine (example I(a)) and 4-[2-[4-(4,4,5,5-

tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-ethyl]-morpholine (prepared in part 1) following procedure 3 as a white solid.

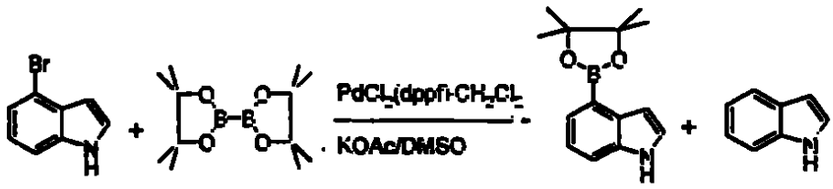
Example I-3:



1. 3-[2-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-ethyl]-morpholine was prepared following the same procedure as 4-[2-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-ethyl]-morpholine in Example I-2 using 3-(4,4,5,5-tetramethyl-1,3-2-dioxabordan-2-yl) phenol in 92% yield as a white wax solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.28 (t, 1H), 7.22 (dt, 1H), 7.14 (d, 1H), 7.04 (ddd, 1H), 4.06 (t, 2H), 3.58 (*m*, 4H), 2.49 (t, 2H), 2.45 (*m*, 4H).

2. 3-(2,6-Dichloro-benzyloxy)-5-[3-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine was prepared from 5-bromo-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine (example I(a)) and 3-[2-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-ethyl]-morpholine prepared in part 1 following procedure 3 as a light yellow solid.

Example I-4:



1. To a mixture of 4-bromoindole (9.80g, 50 mmol), pinacole diborate (13.97g, 55 mmol), and KOAc (14.72g, 150 mmol) in DMSO (200 mL) was added palladium catalyst $PdCl_2(dppf)\cdot CH_2Cl_2$ (1.22g, 1.5 mmol). The system was degassed, and then charged with nitrogen for three times. The mixture was stirred at 80 °C oil bath under nitrogen for 22 hours. TLC showed the complete disappearance of the starting material 4-bromoindole. The mixture was cooled to room temperature, and then poured to water (1 L). The product was extracted with ethyl acetate for three times. The combined extracts were washed by brine for five times to remove DMSO solvent, and then dried over Na_2SO_4. During the washing step, the catalyst may precipitate out, which was removed by filtration. The ethyl acetate solution was filtered and condensed. The residue was purified on a silica gel column eluting with EtOAc-hexane (9:1). The first fraction provided the side product indole (1.25g, 21% yield), R_f 0.55 (EtOAc-Hexane 5:1). The second fraction provided 4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-indole as a white solid (8.01g, 66%), R_f 0.46 (EtOAc-Hexane 5:1). ^{1}H NMR (300 MHz, DMSO-d_6): δ11.03 (bs, 1H, N-H)), 7.49 (d, *J* 7.7 Hz, 1H, H-5), 7.38 (dd, *J* 0.9 Hz, *J* 7.0 Hz, 1H, H-7), 7.38 (t, *J* 2.6Hz, 1H, H-2), 7.06 (dd, *J* 7.7 Hz, *J* 7.0 Hz, 1H, H-6), 6.73 (bd, *J* 2.2 Hz, 1H, H-3), 1.32 (s, 12H, $4CH_3$); MS (*m/e*): 244 $(M+H)^+$.

2. 3-(2,6-dichloro-benzyloxy)-5-(1*H*-indol-4-yl)-pyridin-2-ylamine was prepared from 5-bromo-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine (Example I(a)) and 4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-indole following procedure 3. The first fraction was identified to be 3-(2,6-dichloro-benzyloxy)-5-(1H-indol-4-yl)-pyridin-2-ylamine.

Example I-5: The same experiment was performed as Example 4, and the second fraction was identified as 3-[2-chloro-6-(1*H*-indol-4-yl)-benzyloxy]-5-(1*H*-indol-4-yl)-pyridin-2-ylamine.

Example I-6: 2-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-pyrrole-1-carboxylic acid *tert*-butyl ester was prepared from 5-bromo-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine (Example I(a)) and *N*-Boc pyrrole-2-boronic acid following procedure 3.

Example I-7: To a mixture of 2-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-pyrrole-1-carboxylic acid *tert*-butyl ester (Example 6, 30 mg, 0.069 mmol) in ethanol/water (2:1, 10 mL) was added sodium carbonate (100 mg, 0.95 mmol). The mixture was refluxed overnight. The reaction was cooled to ambient temperature and extracted with ethyl acetate. The mixture was washed with water, brine, dried over Na_2SO_4, and purified on a silica gel column to afford 3-(2,6-dichloro-benzyloxy)-5-(1*H*-pyrrol-2-yl)-pyridin-2-ylamine.

Examples I-8 to I-12: The compounds of Examples 1-8 to I-12 were prepared according to procedure 3 using 5-bromo-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine and: 4-fluorophenyl boronic acid (Example I-8); phenyl boronic acid (Example I-9); 2-fluorophenyl boronic acid (Example I-10); 3-fluorophenyl boronic acid (Example I-11); and 4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenylamine (Example I-12).

Example I-13: To a solution of 5-(4-amino-phenyl)-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine (100 mg, 0.28 mmol) in methylene chloride (5 mL) at 0°C, was added methanesulfonyl chloride (0.021 mL, 0.28 mmol) and 4-methylmorpholine (0.16 mL). The mixture was stirred at room temperature for 2 hr, and diluted with ethyl acetate. The organic layers were washed with brine, dried over sodium sulfate and concentrated. The residue was purified with a silica gel column eluting with hexane-ethyl acetate (5:1) to give *N*-[4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl]-methanesulfonamide.

Example I-14: To a solution of 5-(4-amino-phenyl)-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine (100 mg, 0.28 mmol) in acetonitrile (3 mL) at 0°C, was added pyridine (0.035 mL, 1.5 eq.) and acetic anhydride (0.03 mL, 0.28 mmol). The mixture was stirred at room temperature over night, and the precipitate was filtered to provide *N*-[4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl]-acetamide as a white solid.

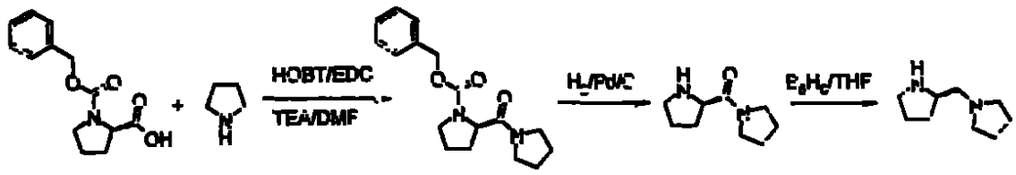
Examples I-15 to I-35: The compounds of Examples I-15 to I-35 were prepared according to procedure 3 from 5-bromo-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine and: 3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenol (Example I-15); 4-methoxyphenyl boronic acid (Example I-16); 3-aminobenzeneboronic acid (Example I-17); 4-trifluoromethoxybenzeneboronic acid (Example I-18); 2-hydroxybenzene boronic acid (Example I-19); 2-phenoxyphenylboronic acid (Example I-20); 3,4-difluorophenylboronic acid. (Example I-21); (3-isopropyl)phenylboronic acid (Example I-22); (2-trifluoromethylphenyl)boronic acid (Example I-23); (2-methoxyphenyl)boronic acid (Example I-24); (4-trifluoromethylphenyl)boronic acid (Example I-25); [(2-methylsulfonylamino)phenyl]boronic acid

(Example I-26); 4-hydroxymethylphenylboronic acid (Example I-27); 3,4-methylenedioxyphenylboronic acid (Example I-28); 2-trifluoromethoxyphenylboronic acid (Example I-29); 4-methylthiophene-2-boronic acid (Example I-30); 2-benzyloxyphenylboronic acid (Example I-31); 3-methoxyphenylboronic acid (Example I-32); 1-(*tert*-butoxycarbonyl)indole-2-boronic acid, and the *tert*-butoxycarbonyl group was removed using 20% trifluoroacetic acid in dichloromethane (Example I-33); (3-fluoro-4-benzyloxyphenyl)boronic acid (Example I-34); and 4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzoic acid (Example I-35).

Example I-36: To a solution of 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid (50 mg, 0.13 mmol), HOBT (21 mg, 0.156 mmol), and EDC (30 mg, 0.156 mmol) in DMF (2 mL) was added *N*, *N*-diethylethylenediamine (0.022 mL, 0.156 mmol). The reaction was stirred at room temperature for 24 hr, then diluted with EtOAc, and partitioned with H_2O. The organic was separated and the aqueous was extracted with EtOAc. The organic layers were combined, washed with saturated $NaHCO_3$, and concentrated to dryness under vacuum. The material was purified using column chromatography (silica gel, 99:1 to 95:5 CH_2Cl_2/MeOH) to give 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-N-(2-diethylamino-ethyl)-benzamide (45 mg, 72% yield) as a white solid.

Examples I-37 and I-38: The compounds of Examples I-37 and I-38 were prepared from 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid and *N*, *N*-diethyl-1,3-propanediamine (Example I-37) and 1-methylpiperazine(Example I-38), following procedure 4.

Example I-39:

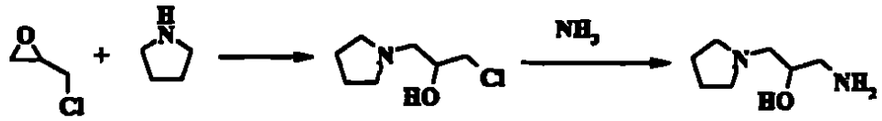


1. A mixture of (+)-carbobenzyloxy-D-proline (1.5 g, 6 mmol), EDC (2.3 g, 12 mmol), HOBt (800 mg, 6 mmol), TEA (1.5 mL) and pyrrolidine (853 mg, 12 mmol) in DMF (20 mL) was stirred at rt for 18 hr. The reaction was diluted with water and sodium bicarbonate, extracted with dichloromethane (3x). The combined DCM was concentrated and purified on a silica gel column to give (*R*)-2-(pyrrolidine-1-carbonyl)-pyrrolidine-1-carboxylic acid benzyl ester. (*R*)-2-(pyrrolidine-1-carbonyl)-pyrrolidine-1-carboxylic acid benzyl ester was hydrogenated using Pd/C in methanol at ambient temperature for 20 hr to provide pyrrolidin-1-yl-(*R*)-pyrrolidin-2-yl-methanone. To a solution of pyrrolidin-1-yl-(*R*)-pyrrolidin-2-yl-methanone (1.2 g, 7.1 mmol) in THF (10 mL) at 0°C was added B_2H_6 (10 mL, 10 mmol). The mixture was heated to reflux for 16 hr. The reaction was acidified with HCl and concentrated. The residue was basified to pH 10 with 2N NaOH and extracted with 5% methanol in DCM. The organic layer was concentrated and purified on a silica gel column to give 800 mg (73%) of (*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine.

2. {4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone was prepared from 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid and (2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine following procedure 4.

Examples I-40 to I-45: The compounds of Examples I-40 to I-45 were prepared according to procedure 4 from 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid and: (2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-40); 4-pyrrolidin-1-yl-piperidine (Example I-41); 4-piperidine ethanol (Example I-42); (3*S*)-(3-dimethylamino-pyrrolidine (Example I-43); (3*R*)-(3-dimethylamino-pyrrolidine (Example I-44); and (*S*)-3-cyclopropylaminomethyl-piperidine (prepared according to the procedures for (*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine in example I-39) (Example I-45).

Example I-46:



1. To a solution of epichlorohydrin (from Aldrich, Milwaukee, 3.91 mL, 50.0 mmol) in EtOH (100 mL) was added pyrrolidine (4.18 mL, 50.0 mmol) at room temperature. The mixture was stirred at 55~60°C for 20 hr, then refluxed for 3 hr. The solvent was removed under reduced pressure and crude 1-chloro-3-pyrrolidin-1-yl-propan-2-ol was obtained as an oil (10 g). This oily product was dissolved in 7 M ammonia in MeOH (40 mL) and stirred at room temperature overnight. Then another 30 mL of 7M ammonia in MeOH was added and the mixture was stirred at 40°C overnight. NMR showed that the starting material disappeared completely. The solvent was removed and the residue was dissolved in 2 N HCl and then lyophilized to give 10.6 g of oil salt product, which was dissolved in MeOH-H_2O at 0°C and the resin (AG1-X8, hydroxide form) was added in portions with stirring until the pH of the solution is above 9.0. After filtration, the filtrate was evaporated under reduced pressure to give the free amine 1-amino-3-pyrrolidin-1-yl-propan-2-ol as yellowish oil (6.6 g). This crude product was used for the reaction without further purification.

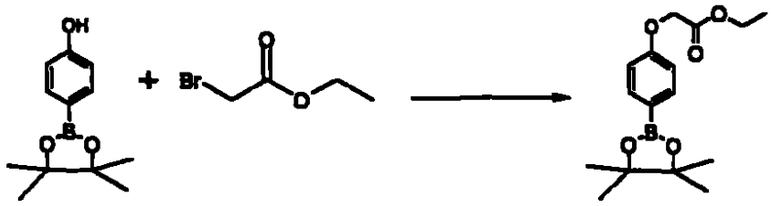
2. 4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-*N*-(2-hydroxy-3-pyrrolidin-1-yl-propyl)-benzamide was prepared from 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid and 1-amino-3-pyrrolidin-1-yl-propan-2-ol following procedure 4.

Examples I-47 to I-52: The compounds of Examples I-47 to I-52 were prepared according to procedure 4 from 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid and: 3-fluoro-1-(2*S*)-pyrrolidin-2-ylmethyl-piperidine (prepared according to the procedures for (*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine) (Example I-47); 1-cyclopropyl-piperazine (Example I-48); (*R*)-2-[(cyclopropylmethyl-amino)-methyl]-pyrrolidine (prepared according to the procedures for (*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine) (first fraction, Example I-49; second fraction, Example I-50); *N*-(2-hydroxy-3-pyrrolidin-1-yl-propyl)-*N*-methyl amine (prepared according to the same procedure as 1-amino-3-pyrrolidin-1-yl-propan-2-ol (Example I-51); and (2*S*)-2-[(3*R*)-3-hydroxy-pyrrolidin-1-ylmethyl)-pyrrolidine (prepared according to the procedure for (*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine) (Example I-52).

Example I-53: 3-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid was prepared from 5-bromo-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine and 3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzoic acid following procedure 3.

Example I-54: {3-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone was prepared from 3-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid and (*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine following procedure 4.

Example I-55:



1. To a solution of 4-(4,4,5,5-tetramethyl-[1,3]dioxolan-2-yl)-phenol (10.0 g, 45.5 mmol) and Cs_2CO_3 (23.5 g, 68.25 mmol) in DMF (60 mL) was added ethyl α-bromoacetate (11.6 g, 68.25 mmol). The mixture was stirred at room temperature for 24 hours, then diluted with ethyl acetate, washed with water, dried over Na_2SO_4. After filtration and evaporation, the residue was dried under high vacuum to provide [4-(4,4,5,5-tetramethyl-[1,3]dioxolan-2-yl)-phenoxy]-acetic acid ethyl ester (12.52 g, 90% yield) as an oil.

2. A mixture of 5-bromo-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine (Example I(a)) (2.2 g, 6.3 mmol), [4-(4,4,5,5-tetramethyl-[1,3]dioxolan-2-yl)-phenoxy]-acetic acid ethyl ester (2.9 g, 1.5 eq.), bis(triphenylphosphine)palladium(II) chloride (136 mg) and sodium carbonate (1.83 g, 3.0 eq.) in ethylene glycol dimethyl ether (30 mL), DMF (5 mL) and water (8 mL) was heated to 90-100°C under nitrogen for 7 hr. The reaction was cooled to rt and diluted with ethyl acetate. The mixture was washed with water, brine, dried and purified on silica column to afford {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenoxy}-acetic acid ethyl ester. This ester was treated with sodium carbonate and water at rt overnight. The reaction was diluted with ethyl acetate. The mixture was washed with water, brine, dried and purified on silica column to afford 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenoxy}-acetic acid.

Example I-56: 2-{4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenoxy}-1-[(2R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-ethanone was prepared from 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenoxy}-acetic acid and (*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine following procedure 4.

Example I-57: 2-{4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenoxy}-1-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-ethanone was prepared from 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenoxy}-acetic acid and (*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidine following procedure 4.

Example I-58: 3-(2,6-Dichloro-benzyloxy)-5-(1*H*-indol-5-yl)-pyridin-2-ylamine was prepared from 5-bromo-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine and indole-5-boronic acid following procedure 3.

Example I-59: To a solution of 3-(2,6-Dichloro-benzyloxy)-5-(1*H*-indol-5-yl)-pyridin-2-ylamine (example I-58, 200 mg, 0.52 mmol) in acetic acid (4 mL) and trifluoroacetic acid (1 mL) was added 1-methyl-4-piperidone (0.32 mL, 2.6 mmol). The solution was refluxing for over night, and evaporated. The residue was dissolved in ethyl acetate, washed with saturated $NaHCO_3$ and brine, dried over

Na_2SO_4, and condensed. The crude product was purified on a silica gel column eluting with dichloromethane-methanol-triethyl amine (95:5:0.1) to provide 3-(2,6-dichloro-benzyloxy)-5-[3-(1-methyl-1,2,3,6-tetrahydro-pyridin-4-yl)-1*H*-indol-5-yl]-pyridin-2-ylamine (103.5 mg, 41% yield) as an orange crystalline solid.

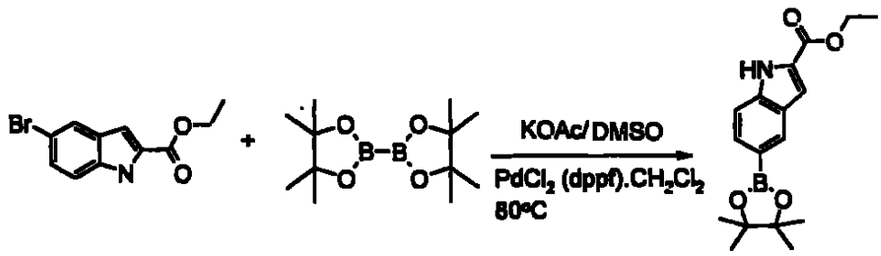
Example I-60: To a de-gassed solution of 3-(2,6-dichloro-benzyloxy)-5-[3-(1-methyl-1,2,3,6-tetrahydro-pyridin-4-yl)-1*H*-indol-5-yl]-pyridin-2-ylamine (example I-61, 130 mg, 0.27 mmol) in methanol (50 mL) and acetic acid (5 mL) was added 10% Pd/C (50 mg). The solution was degassed and charged with hydrogen for three times, and then was stirred under hydrogen balloon for over night. The mixture was filtered through a celite pad, washed with methanol, and then condensed. The residue was dissolved in ethyl acetate, washed with sat. NaHCO3 and brine, dried over Na_2SO_4, and condensed. The crude product was purified on a silica gel column eluting with dichloromethane-methanol-triethyl amine (95:5:0.1) to provide 3-(2,6-dichloro-benzyloxy)-5-[3-(1-methyl-piperidin-4-yl)-1H-indol-5-yl]-pyridin-2-ylamine as a white solid.

Examples I-61-I-68: The compounds of Examples I-61 to I-68 were prepared according to procedure 5 from 3-(2,6-Dichloro-benzyloxy)-5-(1*H*-indol-5-yl)-pyridin-2-ylamine and: morpholine (Example I-61); piperidine (Example I-62); pyrrolidine (Example I-63); diethylamine (Example I-64); pyrrolidin-3-yl-carbamic acid *tert*-butyl ester (Example I-65); 2,6-dimethyl-morpholine following (Example I-66); (*R*)-pyrrolidin-3-yl-acetamide (Example I-67); and piperazin-1-yl-ethanone (Example I-68).

Example I-69: 3-(2-Chloro-3,6-difluoro-benzyloxy)-5-(1*H*-indol-5-yl)-pyridin-2-ylamine was prepared from 5-bromo-3-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-2-ylamine and indole-5-boronic acid following procedure 3.

Examples I-70 to I-75: The compounds of Examples I-70 to I-75 were prepared according to procedure 5 from 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(1*H*-indol-5-yl)-pyridin-2-ylamine and: piperazin-1-yl-ethanone (Example I-70); 2,6-dimethyl-morpholine (Example I-71); (3*S*)-pyrrolidin-3-yl-acetamide (Example I-72); piperidine (Example I-73); morpholine (Example I-74); and pyrrolidine (Example I-75).

Example I-76:



1. To a stirred solution of ethyl 5-bromo-1H-indole-2-carboxylate (5g, 18.6mmol) in DMSO (75mL, 0.25M), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi-1,3,2-dioxaborolane (11.2g, 44.3mmol), potassium acetate (5.5g, 56.0 mmol), and [bis(diphenylphosphino)ferrocene] dichloropalladium II (1.23mmol) were added. The mixture was de-gassed and charged with nitrogen for three times, and then heated at 80°C under nitrogen for overnight. The reaction was cooled to ambient temperature and diluted with ethyl acetate (2x100mL). The mixture was washed with water (1x50 mL), brine (1x50mL), dried over $MgSO_4$,

and purified on a silica gel column to afford ethyl 5-(4,4,5,5-tetramethyl-1, 3,2-dioxaborolan-2-yl)-1*H*-indole-2-carboxylate as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.31 (t, 3H), 4.32 (m, 2H), 7.18 (s, 1H), 7.42 (d, 1H), 7.54 (d, 1H), 8.05 (s, 1H), 11.96 (s, 1H); MS *m/z* 315 (M+1).

2. 5-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carboxylic acid ethyl ester was prepared from 5-bromo-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine and 5-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-1*H*-indole-2-carboxylic acid ethyl ester following procedure 3.

Example I-77: To a mixture of ethyl 5-[6-amino-5- [(2,6-dichlorobenzyl) oxy] pyridin-3-yl]-1*H*-indole-2-carboxylate (2.5 g, 5.5mmol) in methanol:water (60mL:20mL), lithium hydroxide (0.65g, 27.1mmol) was added. The reaction was heated to reflux for overnight. Most of the solvent was evaporated and the mixture was acidified, and stirred for 10 min. The precipitate was filtered out and washed with water to yield 5-[6-amino-5-[(2,6-dichlorobenzyl)oxy]pyridin-3-yl]-1*H*-indole-2-carboxylic acid as tan solid.

Examples I-78 to I-85: The compounds of Examples I-78 to I-85 were prepared according to procedure 4 from 5-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1H-indole-2-carboxylic acid and: *N*-methylpiperazine (Example I-78); (3*R*)-3-dimethylamino-pyrrolidine (Example I-79); (2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (prepared as in example I-39) (Example I-80); 2-pyrrolidin-1-yl-ethylamine (Example I-81); 2-morpholin-4-yl-ethylamine (Example I-82); (*S*)-pyrrolidin-3-yl-carbamic acid *tert*-butyl ester (Example I-83), followed by de-protection of the Boc-group in 20 % trifluoroacetic acid in dichloromethane (Example I-84); 2-hydroxy-3-pyrrolidin-1-yl-propylamine (Example I-85).

Example I-86: 4-(6-Amino-5-benzyloxy-pyridin-3-yl)-phenol was prepared from 3-benzyloxy-5-bromo-pyridin-2-ylamine and 4-(4,4,5,5-tetramethyl-1,3-2-dioxaborolan-2-yl) phenol following procedure 3.

Example I-87: 3-Benzyloxy-5-phenyl-pyridin-2-ylamine was prepared from 3-benzyloxy-5-bromo-pyridin-2-ylamine and phenylboronic acid following procedure 3.

Example I-88: 3-(3-Methoxy-benzyloxy)-5-phenyl-pyridin-2-ylamine was prepared according to procedure 6.

Examples I-89 to I-105: The compounds of Examples I-89 to I-105 were prepared according to procedure 6 from: 2-chloro-4-fluoro-benzylbromide (Example I-89); 2-chlorobenzylbromide (Example I-90); 2,5-dichlorobenzylbromide (Example I-91); 2-chloro-5-trifluoromethyl benzylbromide (Example I-92); 2,4-Dichloro-5-fluoro-benzylbromide (Example I-93); 2-chloro-3-trifluoromethyl-benzylbromide (Example I-94); 2-chloro-3,6difluoro--benzylbromide (Example I-95); 3,4-dichloro-benzylbromide (Example I-96); 2-bromomethyl-benzonitrile (Example I-97); 2-chloro-6-fluoro-3-methyl-benzylbromide (Example I-98); 2-bromomethyl-1,3,4-trifluoro-benzene (Example I-99); 2-bromomethyl-1,3-difluoro-benzene (Example I-100); 2-bromomethyl-1,3-difluoro-4-methyl-benzene (Example I-101); 2-bromomethyl-4-chloro-1,3-difluoro-benzene (Example I-102); 2-bromomethyl-1-chloro-3-fluoro-benzene (Example I-103); 4-bromomethyl-2-fluoro-1-methoxy-benzene (Example I-104); and 1-bromomethyl-3-nitro-benzene, followed by reduction of the nitro group to amino and reaction with methanesulfonyl chloride (Example I-105).

Example I-106: 5-[4-(2-Morpholin-4-yl-ethoxy)-phenyl]-3-(3-nitro-benzyloxy)-pyridin-2-ylamine was synthesized according to procedure 7.

Examples I-107 to I-110: The compounds of Examples I-107 to I-110 were prepared according to procedure 7 from: 1-bromomethyl-naphthalene (Example I-107); 2-bromomethyl-3-chloro-1,4-difluoro-benzene (Example I-108); 2-bromo-*N*-(4-isopropyl-phenyl)-2-phenyl-acetamide (Example I-109); and 3-bromomethyl-5-chloro-benzo[*b*]thiophene (Example I-110).

Example I-111: {4-[6-Amino-5-(4-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone was synthesized according to procedure 8.

Examples I-112 to I-117: The compounds of Examples I-112 to I-117 were prepared according to procedure 8 from: 2-bromomethyl-1-fluoro-3-trifluoromethyl-benzene (Example I-112); 2-bromomethyl-4-fluoro-1-trifluoromethyl-benzene (Example I-113); 1-(1-bromo-ethyl)-2-trifluoromethyl-benzene (Example I-114); 1-bromo-2-bromomethyl-benzene (Example I-115); 1-bromomethyl-3-fluoro-2-trifluoromethyl-benzene (Example I-116); and 2-bromomethyl-3-chloro-1,4-difluoro-benzene (Example I-117).

Examples I-118 to I-121: The compounds of Examples I-118 to I-121 were prepared according to procedure 3 from 5-bromo-3-(2,6-difluoro-benzyloxy)-pyridin-2-ylamine and: 4-(4,4,5,5-tetramethyl-[1,3]dioxolan-2-yl)-phenol (Example I-118); 4-[2-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-ethyl]-morpholine (Example I-119); 4-(4,4,5,5-tetramethyl-[1,3]dioxolan-2-yl)-1*H*-indole (Example I-120); and 4-(4,4,5,5-tetramethyl-[1,3]dioxolan-2-yl)-benzoic acid (Example I-121).

Example I-122: {4-[6-Amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone was prepared from 4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid and (2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine following procedure 4.

Example I-123: {4-[6-Amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone was prepared from 4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid and (2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidine following procedure 4.

Example I-124: {4-[6-Amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenoxy}-acetic acid ethyl ester was prepared from 5-bromo-3-(2,6-difluoro-benzyloxy)-pyridin-2-ylamine and of [4-(4,4,5,5-tetramethyl-[1,3]dioxolan-2-yl)-phenoxy]-acetic acid ethyl ester following procedure 3.

Example I-125: {4-[6-Amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenoxy}-acetic acid ethyl ester (1.0 g, 2.41 mmol) was treated with sodium carbonate (1.28 g, 12.05 mmol) and water (10 mL) at 90-100°C overnight. The reaction was cooled to rt and diluted with ethyl acetate. The mixture was washed with water, brine, dried and purified on silica column to afford 4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenoxy}-acetic acid.

Example I-126: 2-{4-[6-Amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenoxy}-1-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-ethanone was prepared from 4-[6-Amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenoxy}-acetic acid and (2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine following procedure 4.

Example I-127: 2-{4-[6-Amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenoxy}-1-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-ethanone was prepared from 4-[6-Amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenoxy}-acetic acid and (2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidine following procedure 4.

Examples I-128 to I-134: The compounds of Examples I-128 to I-134 were prepared according to procedure 3 from 4-(4,4,5,5-tetramethyl-[1,3]dioxolan-2-yl)-phenol and: 5-bromo-3-(2-chloro-6-fluoro-benzyloxy)-pyridin-2-ylamine (Example I-128); 5-bromo-3-(2-chloro-4-fluoro-benzyloxy)-pyridin-2-ylamine (Example I-129); 5-bromo-3-(2,4-dichloro-benzyloxy)-pyridin-2-ylamine (Example I-130); 2-(2-amino-5-bromo-pyridin-3-yloxymethyl)-benzonitrile (Example I-131); 5-bromo-3-(2-trifluoromethyl-benzyloxy)-pyridin-2-ylamine (Example I-132); 5-bromo-3-(2-chloro-benzyloxy)-pyridin-2-ylamine (Example I-133); and 5-bromo-3-(4-*tert*-butyl -benzyloxy)-pyridin-2-ylamine (Example I-134).

Example I-135:



1. To a solution of 4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenylamine (5.00 g, 22.8 mmol) in methylene chloride (100 mL) and 4-methylmorpholine (16 mL) at 0°C was added methanesulfonyl chloride (2.1 mL, 28 mmol). The mixture was stirred at room temperature for 2 hr, and diluted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate and concentrated to provide *N*-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-methanesulfonamide as a white solid (5.32 g, 83% yield). MS *m/z* 298 (M+1).

2. *N*-[4-[6-Amino-5-(2-cyano-benzyloxy)-pyridin-3-yl]-phenyl]-methanesulfonamide was prepared following procedure 3 from 2-(2-Amino-5-bromo-pyridin-3-yloxymethyl)-benzonitrile and *N*-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-methanesulfonamide.

Example I-136: 10% NaOH solution (25 mL) was added to *N*-[4-[6-amino-5-(2-cyano-benzyloxy)-pyridin-3-yl]-phenyl]-methanesulfonamide (Example I-135, 650 mg, 1.65mmol) in ethylene glycol (55 mL). The mixture was heated to reflux and allowed to stir for 24 hr. The reaction was cooled to room temperature. Most of the solvent was evaporated and the mixture was acidified. The precipitated solid was filtered out to afford 2-[2-Amino-5-(4-methanesulfonylamino-phenyl)-pyridin-3-yloxymethyl]-benzoic acid as light brown solid. The filtrate was neutralized and extracted with EtOAc (5 x 20 mL). The organic layer was combined, dried over $MgSO_4$, and concentrated to yield 2-[2-Amino-5-(4-methanesulfonylamino-phenyl)-pyridin-3-yloxymethyl]-benzamide as an off-white solid.

Example I-137: 2-[2-Amino-5-(4-methanesulfonylamino-phenyl)-pyridin-3-yloxymethyl]-benzoic acid was prepared as in Example I-136.

Example I-138 to I-140: The compounds of Examples I-138 to I-140 were prepared according to procedure 4 from 2-[2-amino-5-(4-methanesulfonylamino-phenyl)-pyridin-3-yloxymethyl]-benzoic acid and: *N*-methyl-piperazine (Example I-138); 2-hydroxyethylamine (Example I-139); and isobutylamine (Example I-140).

Example I-141: 5-Bromo-3-(2-chloro-6-fluoro-benzyloxy)-pyridin-2-ylamine (Example I(e), 8.00 g, 27.0 mmol), 4-carboxybenzeneboronic acid (4.41 g, 27.0 mmol), tetrakis(triphenylphosphine)palladium(0) (0.99 g , 0.9 mmol), potassium carbonate (13.1 g, 95.0 mmol), dimethylformamide (72 mL) and water (36 mL) were charged to a 250 mL three neck round bottom flask equipped with a thermometer, a reflux condenser and magnetic stirring. The mixture was purged with nitrogen and gradually heated from 81°C to 98°C over a period of 4 hr. Thin layer chromatography (ethyl acetate:hexane:acetic acid 4:6:0.5) showed a trace of starting material at Rf 0.7, product at Rf 0.4 and many small impurities. The mixture was cooled to 45°C. The solids were collected by vacuum filtration, washed with 30 mL of ethanol:water 1:1 and discarded. The filtrate was diluted with 432 mL of water and 8 mL of 9 N potassium hydroxide solution (to pH 12-13), cooled in an ice bath and stirred for 30 minutes. The solids were collected by vacuum filtration and washed with 5 mL of water. The filtrate was cooled in an ice bath and acidified to pH 7.5 with acetic acid using a pH meter. The solids were collected by vacuum filtration, washed with 10 mL of ethanol:water 1:1 and dried under vacuum to give 2.5 g of 4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-benzoic acid and a second compound as a brown solid in a ratio of about 1:1 by ^{1}H-NMR. This material was discarded. The filtrate was acidified to pH 6.5 with acetic acid using a pH meter. The solids were collected by vacuum filtration, washed with 10 mL of ethanol:water 1:1 and dried under vacuum to give 3.6 g (36 % yield) of 4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-benzoic acid as a brown solid containing a 5-10 % impurity by ^{1}H-NMR.

Examples I-142 to I-149: The compounds of Examples I-142 to I-149) were prepared according to procedure 4 from 4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-benzoic acid and: (2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-142); (2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-143); (3*S*)-3-dimethylamino-pyrrolidine (Example I-144); (*S*)-pyrrolidin-3-yl-carbamic acid *tert*-butyl ester, followed by de-protection of Boc-group with trifluoroacetic acid in dichloromethane (Example I-145); *N*-methylpiperazine (Example I-146); 1-piperazin-1-yl-ethanone (Example I-147); 2-morpholin-4-yl-ethylamine (Example I-148); 3-morpholin-4-yl-propylamine (Example I-149).

Example I-150: 5-Bromo-3-(2-chloro-benzyloxy)-pyridin-2-ylamine (4.50 g, 14.3 mmol), 4-carboxybenzeneboronic acid (2.62 g, 15.8 mmol), tetrakis(triphenylphosphine)palladium(0) (0.56 g, 0.5 mmol), potassium carbonate (6.90 g, 50 mmol), dimethylformamide (36 mL), and water (18 mL) were charged to a 250 mL three neck round bottom flask equipped with a thermometer, a reflux condenser and magnetic stirring. The mixture was purged with nitrogen and gradually heated from 82 to 93°C over a period of 4 hr. Thin layer chromatography (ethyl acetate:hexane:acetic acid 4:6:0.5) showed product at Rf 0.3 and a few small impurities. The mixture was cooled to 45°C. The solids were collected by vacuum filtration, washed with 10 mL of ethanol:water 1:1 and discarded. The combined filtrate was diluted with 216 mL of water and 4 mL of 9 N potassium hydroxide solution (to pH 12-13), cooled in an ice bath and stirred for 30 minutes with 3 g of Celite and 3 g of Norit. The solids were collected by vacuum filtration through a pad of Celite and washed with 10 mL of water. The solids were discarded. The combined filtrate was cooled in an ice bath and acidified to pH 7 with acetic acid using a pH meter.

The solids were collected by vacuum filtration, washed with 20 mL of ethanol:water 1:1 and dried under vacuum to give 2.7 g (53 % yield) of 4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-benzoic acid.

Examples I-151 to I-159: The compounds of Examples I-151 to I-159 were prepared according to procedure 4 from 4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-benzoic acid and: (2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-151); (2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-152); (3*S*)-3-dimethylamino-pyrrolidine (Example I-153); pyrrolidin-3-yl-carbamic acid *tert*-butyl ester, followed by de-protection of Boc-group with trifluoroacetic acid in dichloromethane (Example I-154); 4-pyrrolidin-1-yl-piperidine (Example I-155); *N*-methylpiperazine (Example I-156); 1-piperazin-1-yl-ethanone (Example I-157); 2-morpholin-4-yl-ethylamine (Example I-158); and 3-morpholin-4-yl-propylamine (Example I-159).

Example I-160: 2-(2-Amino-5-bromo-pyridin-3-yloxymethyl)-benzonitrile (9.0 g, 29.6 mmol), 4-carboxybenzeneboronic acid (5.4 g, 32.5 mmol), tetrakis(triphenylphosphine)palladium(0) (1.1 g, 1.0 mmol), anhydrous potassium carbonate (13.8 g, 70.0 mmol), dimethylformamide (72 mL) and water (36 mL) were charged to a 250 mL three neck round bottom flask equipped with a thermometer, a reflux condenser and magnetic stirring. The mixture was purged with nitrogen and gradually heated from 81 to 90°C over a period of 2 hr. Thin layer chromatography (ethyl acetate:hexane:acetic acid 4:6:0.5) showed a trace of starting material at Rf 0.7, product at Rf 0.4 and an impurity at Rf 0.5. The mixture was cooled to 45°C. The sticky solids were collected by vacuum filtration, washed with 30 mL of ethanol:water 1:1 and discarded. The filtrate was diluted with 432 mL of water and 8 mL of 2 N potassium hydroxide solution (to pH 12-13), cooled in an ice bath and stirred for 30 minutes. The solids were collected by vacuum filtration and washed with 20 mL of water. The solids were discarded. The filtrate was cooled in an ice bath acidified with acetic acid to pH 7.5 using a pH meter. The solids were collected by vacuum filtration, washed with 20 mL water and dried under vacuum to give 8.5 g (83 % yield) of 4-[6-amino-5-(2-cyano-benzyloxy)-pyridin-3-yl]-benzoic acid as a very dark solid.

Examples I-161 to I-170: The compounds of Examples I-161 to I-170 were prepared according to procedure 4 from 4-[6-amino-5-(2-cyano-benzyloxy)-pyridin-3-yl]-benzoic acid and: (2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-161); (2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-162); (3*S*)-3-dimethylamino-pyrrolidine (Example I-163); (*S*)-pyrrolidin-3-yl-carbamic acid *tert*-butyl ester, followed by de-protection of Boc-group with trifluoroacetic acid in dichloromethane (Example I-164); 4-pyrrolidin-1-yl-piperidine (Example I-165); *N*-methylpiperazine (Example I-166); 1-piperazin-1-yl-ethanone (Example I-167); 1-methyl-piperidin-4-ylamine (Example I-168); 2-Morpholin-4-yl-ethylamine (Example I-169); and 3-morpholin-4-yl-propylamine (Example I-170).

Example I-171: 5-Bromo-3-(2,4-dichloro-benzyloxy)-pyridin-2-ylamine (6.96 g, 20.0 mmol), 4-carboxybenzeneboronic acid (3.96 g, 24.0 mmol), tetrakis(triphenylphosphine)-palladium(0) (0.74 g, 0.66 mmol), potassium carbonate (9.7 g, 70 mmol), dimethylformamide (35 mL) and water (17 mL) were charged to a 250 mL three neck round bottom flask equipped with a thermometer, a reflux condenser and magnetic stirring. The mixture was purged with nitrogen and gradually heated from 81 to 95°C over a period of 9 hr. Thin layer chromatography (ethyl acetate:hexane:acetic acid 4:6:0.5) showed a trace of starting material at Rf 0.7, product at Rf 0.4 and impurities at Rf 0.5 and 0.3. The mixture was cooled to room temperature and allowed to stand over for about 48 hr. The solids were collected by vacuum

filtration, washed with 30 mL of ethanol:water 1:1 and saved. The filtrate was diluted with 210 mL of water and 8 mL of 9 N potassium hydroxide solution (to pH 12-13), cooled in an ice bath and stirred for 30 minutes. The solids were collected by vacuum filtration and washed with 5 mL of water to give about 1 g of a mixture of product and a spot running with starting material. This mixture was discarded. The filtrate was cooled in an ice bath and acidified to pH 5-6 with about 10 mL of acetic acid. The solids were collected by vacuum filtration, washed with 10 mL of ethanol:water 1:1 and dried under vacuum to give 2.9 g (37 % yield) of 4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid as a brown solid.

Examples I-172 to I-181: The compounds of Examples I-172 to I-181 were prepared according to procedure 4 from 4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid and: (2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-172); (2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-173); (3*S*)-3-dimethylamino-pyrrolidine (Example I-174); (*S*)-pyrrolidin-3-yl-carbamic acid *tert*-butyl ester, followed by de-protection of Boc-group with trifluoroacetic acid in dichloromethane (Example I-175); 4-pyrrolidin-1-yl-piperidine (Example I-176); *N*-methylpiperazine (Example I-177); 1-piperazin-1-yl-ethanone (Example I-178); 1-methyl-piperidin-4-ylamine (Example I-179); 2-morpholin-4-yl-ethylamine (Example I-180); and 3-morpholin-4-yl-propylamine (Example I-181).

Example I-182: 5-Bromo-3-(2-trifluoromethyl-benzyloxy)-pyridin-2-ylamine (5.80 g, 16.7 mmol), 4-carboxybenzeneboronic acid (3.05 g, 18.4 mmol), tetrakis(triphenylphosphine)-palladium(0) (0.62 g, 0.6 mmol), potassium carbonate (8.10 g, 58 mmol), dimethylformamide (47 mL) and water (23 mL) were charged to a 250 mL three neck round bottom flask equipped with a thermometer, a reflux condenser and magnetic stirring. The mixture was purged with nitrogen and gradually heated from 81 to 93°C over a period of 4 hr. Thin layer chromatography (ethyl acetate:heptane:acetic acid 4:6:0.5) showed product at Rf 0.6 and a few small impurities. The mixture was cooled to 45°C. The solids were collected by vacuum filtration, washed with 10 mL of ethanol:water 1:1 and discarded. The filtrate was diluted with 300 mL of water and 4 mL of 9 N potassium hydroxide solution (to pH 12-13), cooled in an ice bath and stirred for 30 minutes with 3 g of Celite and 3 g of Norit. The solids were collected by vacuum filtration through a pad of Celite and washed with 10 mL of water. The solids were discarded. The filtrate was cooled in an ice bath and acidified to pH 7.3 with acetic acid using a pH meter. The solids were collected by vacuum filtration, washed with 20 mL of ethanol:water 1:1 and dried under vacuum to give 4.5 g (69 % yield) of 4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-benzoic acid as a brown solid.

Examples I-183 to I-192: The compounds of Examples I-183 to I-192 were prepared according to procedure 4 from 4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-benzoic acid and: (2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-183); (2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-184); (3*S*)-3-dimethylamino-pyrrolidine (Example I-185); pyrrolidin-3-yl-carbamic acid *tert*-butyl ester, followed by de-protection of Boc-group with trifluoroacetic acid in dichloromethane (Example I-186); 4-pyrrolidin-1-yl-piperidine (Example I-187); *N*-methylpiperazine (Example I-188); 1-piperazin-1-yl-ethanone (Example I-189); 1-methyl-piperidin-4-ylamine (Example I-190); 2-morpholin-4-yl-ethylamine (Example I-191); and 3-morpholin-4-yl-propylamine (Example I-192).

Example I-193: 2-(2-Amino-5-bromo-pyridin-3-yloxymethyl)-benzonitrile (9.0 g, 26.8 mmol), 4-carboxybenzeneboronic acid (4.9 g, 30.0 mmol), tetrakis(triphenylphosphine)-palladium(0) (1.1 g, 1.0 mmol), anhydrous potassium carbonate (13.1 g, 95 mmol), dimethylformamide (72 mL), and water (36 mL) were charged to a 250 mL three neck round bottom flask equipped with a thermometer, a reflux condenser and magnetic stirring. The mixture was purged with nitrogen and gradually heated from 81 to 98°C over a period of 2 hr. Thin layer chromatography (ethyl acetate:hexane:acetic acid 4:6:0.5) showed a trace of starting material at Rf 0.8, product at Rf 0.5 and an impurity at Rf 0.4. The mixture was cooled to 45°C and filtered to remove the solids. The filtrate was diluted with 432 mL of water and 8 mL of 9 N potassium hydroxide solution (to pH 12-13), cooled in an ice bath and 4 g of Celite and 2 g of Norit were added. The solids were collected by vacuum filtration through 4 g of Celite, washed with 30 mL of ethanol:water 1:1 and discarded. The filtrate was cooled in an ice bath and acidified with acetic acid to pH 7.5 using a pH meter. The solids were collected by vacuum filtration, washed with 20 mL water and dried under vacuum to give 8.1 g (80 % yield) 4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-benzoic acid as a dark solid.

Examples I-194 to I-201: The compounds of Examples I-194 to I-201 were prepred according to procedure 4 from 4-[6-Amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-benzoic acid and: (2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-194); (2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-195); (3*S*)-3-dimethylamino-pyrrolidine (Example I-196); *N*-methylpiperazine (Example I-197); 1-piperazin-1-yl-ethanone (Example I-198); 1-methyl-piperidin-4-ylamine (Example I-199); 2-morpholin-4-yl-ethylamine (Example I-200); and 3-morpholin-4-yl-propylamine (Example I-201).

Example I-202: 5-Bromo-3-(2-chloro-4-fluoro-benzyloxy)-pyridin-2-ylamine (9.00 g, 27.0 mmol), 4-carboxybenzeneboronic acid (4.41 g, 27.0 mmol), tetrakis(triphenylphosphine)-palladium(0) (0.99 g, 0.9 mmol), potassium carbonate (13.1 g, 95 mmol), dimethylformamide (72 mL), and water (36 mL) were charged to a 250 mL three neck round bottom flask equipped with a thermometer, a reflux condenser and magnetic stirring. The mixture was purged with nitrogen and gradually heated from 81 to 98°C over a period of 4 hr. Thin layer chromatography (ethyl acetate:hexane:acetic acid 4:6:0.5) showed a trace of starting material at Rf 0.7, product at Rf 0.4 and a few small impurities. The mixture was cooled to 45°C. The solids were collected by vacuum filtration, washed with 20 mL of ethanol:water 1:1 and discarded. The filtrate was diluted with 432 mL of water and 8 mL of 9 N potassium hydroxide solution (to pH 12-13), cooled in an ice bath and stirred for 30 minutes. The solids were collected by vacuum filtration and washed with 5 mL of water to give about 1 g of a mixture which was discarded. The filtrate was cooled in an ice bath and acidified to pH 6.5 with acetic acid using a pH meter. The solids were collected by vacuum filtration, washed with 10 mL of ethanol:water 1:1 and dried under vacuum to give 3.8 g (36 % yield) 4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-benzoic acid as a brown solid.

Examples I-203 to I-210: The compounds of Examples I-203 to I-210 were prepared according to procedure 4 from 4-[6-Amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-benzoic acid and: (2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-203); (2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-204); (3*S*)-3-dimethylamino-pyrrolidine (Example I-205); (*S*)-pyrrolidin-3-yl-carbamic acid *tert*-butyl ester,

followed by de-protection of Boc-group with trifluoroacetic acid in dichloromethane (Example I-206); *N*-methylpiperazine (Example I-207); 1-piperazin-1-yl)-ethanone (Example I-208); 2-morpholin-4-yl-ethylamine (Example I-209); and 3-morpholin-4-yl-propylamine (Example I-210).

Example I-211: 4-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid methyl ester was prepared following procedure 3 from 5-bromo-3-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-2-ylamine and 4-methoxycarbonylbenzeneboronic acid as an off-white solid in 55% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ3.94 (s, 3H), 4.79 (bra, 2H), 5.29-5.30 (d, 2H, *J*, 1.6), 7.06-7.19 (dt, 1H, *J*, 4.1, 9.0), 7.2-7.26 (m, 1H), 7.37-7.38 (d, 1H, 1.8), 7.58-7.61 (m, 2H), 8.01-8.02 (d, 2H, *J*, 1.8), 8.08-8.11 (m, 2H).

To a stirred solution of 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid methyl ester (2.5 g, 6 mmol) in warm isopropanol (300 mL) was added H_2O (100 mL) containing LiOH (0.74 g, 31 mol). The reaction immediately turned orange and was left to stir at room temperature for 18 hr. The reaction was diluted with EtOAc (200 mL) and brine (50 mL). The organic was separated off and the aqueous was extracted with EtOAc (2 x 50 mL). The organic layers were combined and washed with brine (2 x 25 mL), dried with Na_2SO_4 and concentrated to dryness under vacuum to yield 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid (2.4 g, 6 mmol, 98%) as an off-white solid.

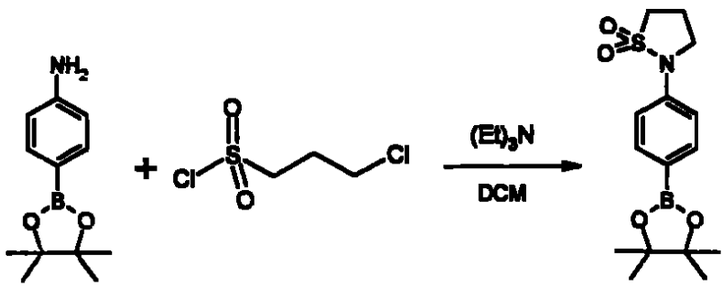
Examples I-212 to I-224: The compounds of Examples I-212 to I-224 were prepared according to procedure 4 from 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid and: *N*-methylpiperazine (Example I-212); 4-pyrrolidin-1-yl-piperidine (Example I-213); piperidin-4-yl-carbamic acid *tert*-butyl ester, followed by de-protection of Boc-group with trifluoroacetic acid in dichloromethane (Example I-214); 3,5-dimethyl-piperazine (Example I-215); (2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-216); (3*S*)-3-dimethylamino-pyrrolidine (Example I-217); (*R*)-pyrrolidin-3-yl-carbamic acid *tert*-butyl ester, followed by de-protection of Boc-group with trifluoroacetic acid in dichloromethane (Example I-218); (*S*)-pyrrolidin-3-yl-carbamic acid *tert*-butyl ester, followed by de-protection of Boc-group with trifluoroacetic acid in dichloromethane (Example I-219); 1-methyl-piperidin-4-ylamine (Example I-220); 2-pyrrolidin-1-yl-ethylamine (Example I-221); 3-pyrrolidin-1-yl-propylamine (Example I-222); 2-morpholin-4-yl-ethylamine (Example I-223); and 3-morpholin-4-yl-propylamine (Example I-224).

Example I-225: 3-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid was prepared using the same procedure as 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid from from 5-bromo-3-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-2-ylamine and 3-methoxycarbonylbenzeneboronic acid.

Examples I-226 to I-239: The compounds of Examples I-226 to I-239 were prepared according to procedure 4 from 3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid and: *N*-methylpiperazine (Example I-226); 4-pyrrolidin-1-yl-piperidine (Example I-227); piperidin-4-yl-carbamic acid *tert*-butyl ester, and then followed by de-protection of Boc-group with trifluoroacetic acid in dichloromethane (Example I-228); 3,5-dimethyl-piperazine (Example I-229); (2S)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-230); (3*S*)-3-dimethylamino-pyrrolidine (Example I-231); (*R*)-pyrrolidin-3-yl-carbamic acid *tert*-butyl ester, followed by de-protection of Boc-group with trifluoroacetic acid in dichloromethane (Example I-232); (*S*)-pyrrolidin-3-yl-carbamic acid *tert*-butyl ester, followed by de-

protection of Boc-group with trifluoroacetic acid in dichloromethane (Example I-233); 1-methyl-piperidin-4-ylamine (Example I-234); 2-pyrrolidin-1-yl-ethylamine (Example I-235); 3-pyrrolidin-1-yl-propylamine (Example I-236); 2-morpholin-4-yl-ethylamine (Example I-237); 3-morpholin-4-yl-propylamine (Example I-238); and 1-[4-(2-amino-ethyl)-piperazin-1-yl]-ethanone (Example I-239).

Example I-240:



1. 4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (5 g, 22.8 mmol) was dissolved in DCM (100 mL, 0.2M), triethylamine (15 mL, 5.0 molar equivalent) was added to the mixture. The reaction was stirred at 0°C for 5 min. 3-chloropropane-1-sulfonyl chloride (4.2 g, 23.0 mmol) was added portion wise. The reaction was stirred at 0°C for 1 hr and brought gradually to room temperature, heated to reflux at 70°C for 2 hr. The mixture was cooled to room temperature, diluted with EtOAc and water. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified through a silica column to afford 2-[4-(4,4,5,5-tetramethyl-1, 3,2-dioxaborolan-2-yl)phenyl]isothiazolidine 1,1-dioxide as off-white solid (5.2 g, 70% yield). ^1H NMR (400 MHz, DMSO-d_6) δ 7.62 (d, 2H), 7.18 (d, 2H), 3.76 (t, 2H), 3.53 (t, 2H), 2.41 (t, 2H), 1.28 (s, 12H).

2. 3-(2-Chloro-3,6-difluoro-benzyloxy)-5-[4-(1,1-dioxo-1λ^6-isothiazolidin-2-yl)-phenyl]-pyridin-2-ylamine was prepared following procedure 3 from 5-bromo-3-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-2-ylamine and 2-[4-(4,4,5,5-tetramethyl-1, 3,2-dioxaborolan-2-yl)phenyl]isothiazolidine 1,1-dioxide.

Example I-241: 3-(2,6-Dichloro-benzyloxy)-5-[4-(1,1-dioxo-1λ^6-isothiazolidin-2-yl)-phenyl]-pyridin-2-ylamine was prepared following procedure 3 from 5-bromo-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine and 2-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]iso-thiazolidine 1,1-dioxide.

Example I-242: 5-[4-(1,1-dioxo-1λ^6-isothiazolidin-2-yl)-phenyl]-3-(2-fluoro-6-trifluoromethyl-benzyloxy)-pyridin-2-ylamine was prepared according to procedure 8.

Example I-243: 2-Diethylamino-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide was synthesized according to procedure 9.

Examples I-244 to I-266: The compounds of Examples I-244 to I-266 were prepared following procedure 9.

Examples I-267 to I-269: The compounds of Examples I-267 to I-269 were prepared according to procedure 3, with purification by reversed phase preparative HPLC eluting with acetonitrile-water-trifluoroacetic acid system and obtained as trifluoroacetic acid salts, from 5-bromo-3-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-2-ylamine and: 2-(dimethylaminomethyl)-phenylboronic acid (Example I-267);

3-(pyrrolidin-1-yl)-phenylboronic acid (Example I-288) and *N*-[4-(4,4,5,5-tetramethyl-[1.3,2]dioxaborolan-2-yl)-phenyl]-methanesulfonamide (Example I-289).

Example I-270: 5-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophene-2-carboxylic acid was prepared following procedure 3 starting from 5-bromo-3-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-2-ylamine and 5-carboxythiophene-2-boronic acid.

Examples I-271 to I-276: Examples I-271 to I-276 were prepared according to procedure 4 from 5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophene-2-carboxylic acid and: *N*-methylpiperazine (Example I-271); (2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-272); 1-methyl-piperidin-4-yl)-amine (Example I-273); 3,5-dimethyl-piperazine (Example I-274); 2-pyrrolidin-1-yl-ethylamine (Example I-275); and 4-pyrrolidin-1-yl-piperidine (Example I-276).

Example I-277: 4-[6-Amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-benzoic acid was prepared using the same procedure as 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid from 5-bromo-3-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-2-ylamine and 4-methoxycarbonylbenzeneboronic acid.

Examples I-278 to I-285: Examples I-278 to I-285 were prepared according to procedure 4 from 4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-benzoic acid and: 4-pyrrolidin-1-yl-piperidine (Example I-278); 1-methyl-piperidin-4-ylamine (Example I-279); 3,5-dimethyl-piperazine (Example I-280); 3-dimethylamino-pyrrolidine (Example I-281); (2S)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-282); 2-morpholin-4-yl-ethylamine (Example I-283); *N*-methylpiperazine (Example I-284); and 4-acetyl-piperazin-1-yl)-ethylamine (Example I-285).

Examples I-286 to I-289: The compounds of Examples I-286 to I-289 were prepared following procedure 9.

Example I-290: 4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid was prepared using the same procedure as 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid from 5-bromo-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine and 4-methoxycarbonylbenzeneboronic acid.

Examples I-291 to I-296: The compounds of Examples I-291 to I-296 were prepared according to procedure 4 from 4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid and: (2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example I-291); 1-methyl-piperidin-4-ylamine (Example I-292); (*R*)-pyrrolidin-3-yl-carbamic acid *tert*-butyl ester, followed by de-protection of Boc-group with trifluoroacetic acid in dichloromethane (Example I-293); 4-pyrrolidin-1-yl-piperidine (Example I-294); *N*-methyl-piperazine (Example I-295); and 3,5-dimethyl-piperazine (Example I-296).

Examples I-297 to I-299: The compounds of Examples I-297 to I-299 were prepared following procedure 9.

Examples I-300 to I-661 were prepared according to the procedures referenced in the Tables herein, except as specifically described in the following paragraphs. When multiple procedures are referenced in the Tables separated by "/", the indicated procedures were performed sequentially.

Example I-311: 3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid was prepared using the same procedure as 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-

benzoic acid from 5-bromo-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine and 3-methoxycarbonylbenzeneboronic acid.

Example I-312: 3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone was prepared following procedure 4 starting from 3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid and 1-methyl-piperidin-4-ylamine.

Example I-330: 4-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid was prepared using the same procedure as 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid from 5-bromo-3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-2-ylamine and 4-methoxycarbonylbenzeneboronic acid.

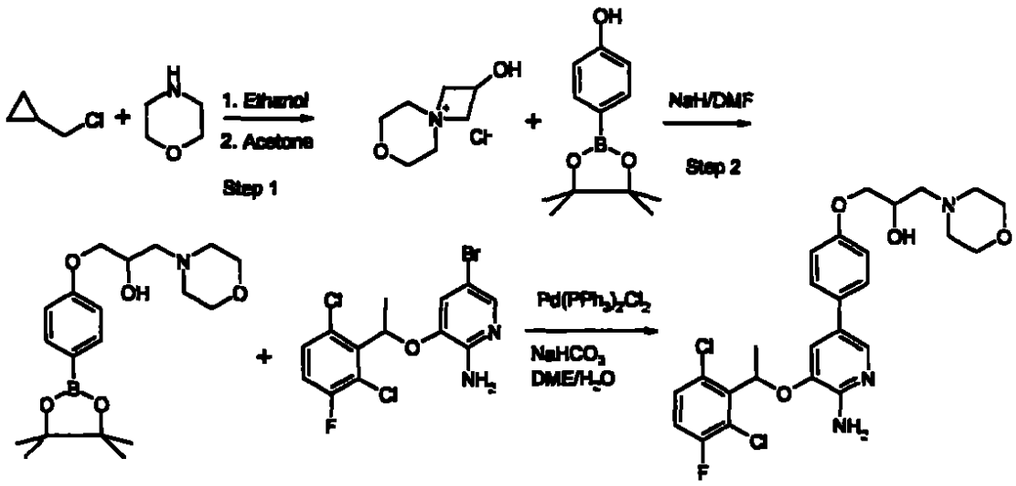
Example I-331: 4-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide was prepared following procedure 4 starting from 4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid and the corresponding amine.

Example I-342: 3-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid was prepared using the same procedure as 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid from 5-bromo-3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-2-ylamine and 3-methoxycarbonylbenzeneboronic acid.

Example I-343: (3-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone was prepared following procedure 4 starting from 3-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid and the corresponding amine.

Example I-359:

1. Preparation of 2-hydroxy-7-oxa-4-aza-spiro[3.5]nonane: To a solution of morpholine (17.4 mL, 0.2 mol, 1.0 eq.) in ethanol (20 mL) was added epichlorohydrin (15.1 ml, 1.03 eq.) from the addition funnel. The reaction was cooled with an ice water bath and gradually raised to room temperature. After 24 hr, the reaction was concentrated at 50°C until no more distillate could be condensed. The resulting oil was stored at room temperature for 24-48 hr or until a significant mass of crystals was observed. The slurry was diluted with acetone and filtered. The solids were dried under high vacuum. This provided 20g of crystalline product. The mother liquors could be concentrated and the crystallization process repeated to increase recovery.



2. Preparation of 1-Morpholin-4-yl-3-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-propan-2-ol: 4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenol (440 mg, 2mmol) was added to a stirred suspension of NaH (96mg, 2eq) in DMF (10mL) at 0°C. After 1 hr, 2-hydroxy-7-oxa-4-azonia-spiro[3.5]nonane (714mg, 2eq.) was added. The mixture was stirred at room temperature overnight. The reaction mixture was poured into sat'd NH_4Cl solution, and extracted with ethyl acetate. The extracts were washed with brine, dried over Na_2SO_4 and condensed to dryness. The crude product was purified with a silica gel column eluting with 2% methanol in methylene chloride to afford 220mg of product as a pink solid (30%). ^1H NMR (400 MHz, DMSO-d_6): δ 7.58 (d, J = 8.2 Hz, 2H), 6.915 (d, J = 7.8 Hz, 2H), 4.89 (d, J = 2.0 Hz, 1H), 3.95 (m, 3H), 3.55 (m, 4H), 2.40 (m, 6H), 1.27 (s, 12H). MS (m/e): 364 $[M+H]^+$ (100%).

3. 1-(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenoxy)-3-morpholin-4-yl-propan-2-ol was prepared following procedure 3 starting from 5-bromo-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine and 1-morpholin-4-yl-3-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-propan-2-ol.

Example I-371: 4-Methyl-piperazine-1-carboxylic acid (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide was prepared according to procedure 10.

Example I-366: 3-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-benzoic acid was prepared using the same procedure as 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid from 5-bromo-3-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-2-ylamine and 3-methoxycarbonylbenzeneboronic acid.

Example I-387: (3-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone was prepared following procedure 4 starting from 3-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-benzoic acid and 3,5-dimethyl-piperazine.

Example 388: 4-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-benzoic acid was prepared using the same procedure as 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-

benzoic acid from 5-bromo-3-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-2-ylamine and 4-methoxycarbonylbenzeneboronic acid .

Example 400: 4-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide was prepared following procedure 4 starting from 4-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid and 2-pyrrolidin-1-yl-ethylamine.

Example I-454:



To a solution of 5-bromo-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine (5.00 g, 13.15 mmol) in DMF (73 mL) and water (1 mL) was added $Zn(CN)_2$ (4.50 g, 26.3 mmol), $Pd_2(dba)_3$ (0.602 g, 0.65 mmol), and DPPF (0.86 g, 1.55 mmol). The mixture was degassed and charged with nitrogen for three time, and then stirred under nitrogen at 100°C for 3 hr. The reaction solution was partitioned between ethyl acetate and water. The organic layer was washed with a solution of sat. NH_4Cl-conc. NH_4OH-water (4:1:4), then dried over $MgSO_4$. The crude product was purified on a silica gel column eluting with ethyl acetate-hexanes (1:4) to provide 6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-nicotinonitrile as a white solide (4.15 g, 97% yield).

Example I-455: 6-Amino-5-[1-(2,6-dichloro-3-cyano-phenyl)-ethoxy]-nicotinonitrile was obtained as a side product from the preparation of 6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-nicotinonitrile.

Example I-456: 5-Aminomethyl-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine was prepared with the reduction of 6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-nicotinonitrile. To a solution of borane in THF (1.0 M, 16.8 mL, 16.8 mmol) was added 6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]nicotinonitrile (785 mg, 2.41 mmol) in anhydrous THF (8 mL) at 0°C under nitrogen. The reaction solution was stirred under nitrogen at 0°C for 5 hr, and then HCl solution (6N, 12 mL) was added slowly followed with the addition of water (12 mL) and methanol (80 mL). The mixture was stirred for overnight. After evaporation of solvents, the residue was partitioned between dichloromethane and NaOH solution (1 N). The water layer was extracted for three times, and the combined extracts were dried over $MgSO_4$. After filtration, evaporation and high vacuum dry, a white solid product was obtained (750 mg, 94% yield).

Example I-457: (R)-2-Pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid {6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-ylmethyl}-amide was prepared with the same procedure as Step 4 in procedure 11.

Example I-482: (S)-1-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-ethane-1,2-diol was prepared as follow: To a solution of asymmetic dihydroxylation-mix α (2.33 g) in a 1:1 mixture of t-BuOH and water (8 mL each) cooled to 0°C was added 3-[1-(2,6-dichloro-3-fluoro-phenyl)-

ethoxy]-5-vinyl-pyridin-2-ylamine (500 mg, 1.67 mmol). The reaction mixture was stirred at 0°C until consumption of the starting material. Three more loadings of AD-mix α was added periodically to increase the reaction rate. Water was added (5 mL) and the mixture was extracted with EtOAc (3 x 20 mL). The combined organic layer was dried over Na_2SO_4, and concentrated. The crude product was purified by reverse phase HPLC to provide (S)-1-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-ethane-1,2-diol (320 mg, 53% yield).

Example I-463: (R)-1-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-ethane-1,2-diol was prepared with the same procedure as Example I-462 with AD-mix α.

Examples II-1 to II-6: The compounds of Examples II-1 to II-6 were prepared according to the Suzuki coupling procedure 3 from 5-bromo-3-(2,6-dichloro-benzyloxy)-pyrazin-2-ylamine and: 4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenol (Example II-1); 2-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]isothiazolidine 1,1-dioxide (Example II-2); 3-[2-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-ethyl]-morpholine (Example II-3); 4-[2-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-ethyl]-morpholine (Example II-4); 4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenylamine (Example II-5); and 4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzoic acid (Example II-6).

Example II-7: {4-[5-Amino-6-(2,6-dichloro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone was prepared following the amidation procedure 4 from 4-[5-amino-6-(2,6-dichloro-benzyloxy)-pyrazin-2-yl]-benzoic acid and (2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine.

Example II-8: {4-[5-Amino-6-(2,6-dichloro-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone was prepared following the amidation procedure 4 from 4-[5-amino-6-(2,6-dichloro-benzyloxy)-pyrazin-2-yl]-benzoic acid and 4-pyrrolidin-1-yl-piperidine.

Examples II-9 to II-32: The compounds of Examples II-9 to II-32 were prepared following the Suzuki coupling procedure 3 from 5-bromo-3-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-ylamine and the following compounds prepared according to the procedure in Example I-243: 2-morpholin-4-yl-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-9); 2-piperidin-1-yl-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-10); 2-(4-hydroxy-piperidin-1-yl)-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-11); 2-pyrrolidin-1-yl-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-12); 2-[(3*R*)-3-Hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-13); 2-[(2*S*)-2-Hydroxymethyl-pyrrolidin-1-yl]-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-14); 2-(cyclopropylmethyl-amino)-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-15); 2-dimethylamino-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-16); 2-diethylamino-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-17); 2-(4-acetyl-piperazin-1-yl)-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-18); 2-[4-(2-hydroxy-acetyl)-piperazin-1-yl]-ethanesulfonic acid [4-(4,4,5,5-

tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-19); 2-cyclopropylamino-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-20); 2-[(3*R*)-2-Hydroxymethyl-pyrrolidin-1-yl]-ethanesulfonic acid [3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-21); 2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid [3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-22); 2-(4-acetyl-piperazin-1-yl)-ethanesulfonic acid [3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-23); 2-piperidin-1-yl - ethanesulfonic acid [3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-24); 2-diethylamino-ethanesulfonic acid [3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-25); 2-morpholin-4-yl-ethanesulfonic acid [3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-26); 2-pyrrolidin-1-yl-ethanesulfonic acid [3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-27); 2-dimethylamino-ethanesulfonic acid [3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-28); 2-[4-(2-hydroxy-acetyl)-piperazin-1-yl]-ethanesulfonic acid [3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-29); 2-(cyclopropylmethyl-amino)-ethanesulfonic acid [3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-30); 2-[(3*R*)-3-hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid [3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-31); and 2-cyclopropylamino-ethanesulfonic acid [3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (Example II-32).

Example II-33: 4-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-benzoic acid was prepared following the Suzuki coupling procedure 3 from 5-bromo-3-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-ylamine and 4-(4,4,5,5-tetramethyl-[1,3,2]dioxa-borolan-2-yl)-benzoic acid.

Example II-34: {4-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone was prepared following the amidation procedure 4 from 4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-benzoic acid and (2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine.

Examples II-35 to II-46: The compounds of Examples II-35 to II-46 were prepared according to the amidation procedure 4 from 4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-benzoic acid and: 2-pyrrolidin-1-yl-ethylamine (Example II-35); (S)-pyrrolidin-3-yl-carbamic acid *tert*-butyl ester, followed by de-protection of Boc-group with trifluoroacetic acid in dichloromethane (Example II-36); 1-[4-(2-amino-ethyl)-piperazin-1-yl]-ethanone (Example II-37); 3-pyrrolidin-1-yl-propylamine (Example II-38); (3*S*)-3-dimethylamino-pyrrolidine (Example II-39); (R)-pyrrolidin-3-yl-carbamic acid *tert*-butyl ester, followed by de-protection of Boc-group with trifluoroacetic acid in dichloromethane (Example II-40); 3,5-dimethyl-piperazine (Example II-41); 4-pyrrolidin-1-yl-piperidine (Example II-42); 3-morpholin-4-yl-propylamine (Example II-43); 1-methyl-piperidin-4-ylamine (Example II-44); 2-morpholin-4-yl-ethylamine (Example II-45); and *N*-methylpiperazine (Example II-46).

Example II-47: 3-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-benzoic acid was prepared following the Suzuki coupling procedure 3 from 5-bromo-3-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-ylamine (Example II(b)) and 3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzoic acid (Aldrich, Milwaukee).

Examples II-48 to II-60: The compounds of Examples II-48 to II-60 were prepared according to the amidation procedure 4 from 3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-benzoic acid and: N-methylpiperazine (Example II-48); (*R*)-pyrrolidin-3-yl-carbamic acid *tert*-butyl ester, followed by de-protection of Boc-group with trifluoroacetic acid in dichloromethane (Example II-49); (*S*)-pyrrolidin-3-yl-carbamic acid *tert*-butyl ester, followed by de-protection of Boc-group with trifluoroacetic acid in dichloromethane (Example II-50); 3,5-dimethyl-piperazine (Example II-51); 3-morpholin-4-yl-propylamine (Example II-52); 4-pyrrolidin-1-yl-piperidine (Example II-53); (3*S*)-3-dimethylamino-pyrrolidine (Example II-54); 2-pyrrolidin-1-yl-ethyl amine (Example II-55); 1-methyl-piperidin-4-ylamine (Example II-56); (2*S*)-pyrrolidin-1-ylmethyl-pyrrolidine (Example II-57); 2-morpholin-4-yl-ethylamine (Example II-58); 2-(4-Acetyl-piperazin-1-yl)-ethylamine (Example II-59); and 3-pyrrolidin-1-yl-propylamine (Example II-60).

Example II-61: 3-(2-Chloro-3,6-difluoro-benzyloxy)-5-(1*H*-indol-5-yl)-pyrazin-2-ylamine was prepared from 6-bromo-3-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-ylamine and indole-5-boronic acid following procedure 3.

Examples II-62 to II-68: The compounds of Examples II-62 to II-68 were prepared according to procedure 5 from 3-(2-Chloro-3,6-difluoro-benzyloxy)-5-(1*H*-indol-5-yl)-pyrazin-2-ylamine and: *pyrrolidine* (Example II-62); *diethylamine* (Example II-63); 1-piperazin-1-yl-ethanone (Example II-64); 2,6-dimethyl-morpholine (Example II-65); *N*-(*S*)-pyrrolidin-3-yl-acetamide (Example II-66); piperidine (Example II-67); and morpholine (Example II-68).

Example II-69: 3-[1-(2-Chloro-3,6-difluoro-phenyl)-2-methyl-propoxy]-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyrazin-2-ylamine was prepared following the Suzuki coupling procedure 3 from 5-bromo-3-[1-(2-chloro-3,6-difluoro-phenyl)-2-methyl-propoxy]-pyrazin-2-ylamine and 4-[2-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-ethyl]-morpholine.

Example II-70: (3-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyrazin-2-ylamine, compound with trifluoro-acetic acid, was prepared following the Suzuki coupling procedure 3 from 5-bromo-3-[1-(2-chloro-3,6-difluoro-phenyl)-2-methyl-propoxy]-pyrazin-2-ylamine and 4-[2-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-ethyl]-morpholine. The product was purified with a reversed phase C-18 preparative HPLC eluting with acetonitrile-water-trifluoroacetic acid and obtained as a trifluoroacetic acid salt.

Examples II-71 to II-83: The compounds of Examples II-71 to II-83 were prepared according to the Suzuki coupling procedure 3 from 5-bromo-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-ylamine and: 4-[2-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-ethyl]-morpholine, followed by purification with a reversed phase C-18 preparative HPLC eluting with acetonitrile-water-trifluoroacetic acid and obtained as a trifluoroacetic acid salt (Example II-71); *N*-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-methane-sulfonamide (Example II-72); 2-pyrrolidin-1-yl -ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (prepared as in Example I-243) (Example II-73); 2-(4-hydroxy-piperidin-1-yl)-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (prepared as in Example I-243) (Example II-74); 2-piperidin-1-yl-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (prepared according to the procedure in Example I-243) (Example II-75); 2-(cyclopropylmethyl-amino)-ethanesulfonic acid [4-

(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (prepared as in Example I-243) (Example II-76); 2-[(3*R*)-3-Hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (prepared as in Example I-243) (Example II-77); 2-[(2*S*)-2-Hydroxymethyl-pyrrolidin-1-yl]-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (prepared as in Example I-243) (Example II-78); 2-dimethylamino-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (prepared as in Example I-243) (Example II-79); 2-morpholin-4-yl-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (prepared as in Example I-243) (Example II-80); 2-diethylamino-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (prepared as in Example I-243) (Example II-81); 2-cyclopropylamino-ethanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (prepared as in Example I-243); and 3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzoic acid (Example II-83).

Examples II-84 to II-88: The compounds of Examples II-84 to II-88 were prepared according to the amidation procedure 4 from 3-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-benzoic acid and: (*S*)-pyrrolidin-3-yl-carbamic acid *tert*-butyl ester, followed by de-protection of Boc-group with trifluoroacetic acid in dichloromethane (Example II-84); (*R*)-pyrrolidin-3-yl-carbamic acid *tert*-butyl ester, followed by de-protection of Boc-group with trifluoroacetic acid in dichloromethane (Example II-85); (2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine (Example II-86); 2-(4-acetyl-piperazin-1-yl)-ethylamine (Example II-87); and (2*S*)-pyrrolidin-1-ylmethyl-pyrrolidine (Example II-88).

Example II-89: 3-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-benzoic acid was prepared following the Suzuki coupling procedure 3 from 5-bromo-3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-ylamine and 3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzoic acid.

Example II-90: 3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide was prepared following the amidation procedure 4 from 3-[5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-benzoic acid and 1-methyl-piperidin-4-ylamine.

Example II-91: 3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-*N*-(3-pyrrolidin-1-yl-propyl)-benzamide was prepared following the amidation procedure 4 from 3-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-benzoic acid and 3-pyrrolidin-1-yl-propylamine.

Example II-92: (3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone was prepared following the amidation procedure 4 from 3-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-benzoic acid and 4-pyrrolidin-1-yl-piperidin-1-ylamine.

Example II-93: 4-[5-Amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-benzoic acidwas prepared following the Suzuki coupling procedure 3 from 5-bromo-3-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-ylamine and 3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzoic acid.

Example II-94: 4-[5-Amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide was prepared following the amidation procedure 4 from 4-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-benzoic acid and 2-morpholin-4-yl-ethylamine.

Example II-95: 4-[5-Amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide was prepared following the amidation procedure 4 from 4-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-benzoic acid and 1-methyl-piperidin-4-ylamine.

Examples II-96 to II-211 were prepared according to the procedures referenced in the Tables herein, except as specifically described in the following paragraphs.

Example II-108: 4-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-benzoic acid was prepared using the same procedure as 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid from 5-bromo-3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-ylamine and 4-methoxycarbonylbenzeneboronic acid.

Example II-109: 4-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide was prepared following procedure 4 starting from 4-[5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-benzoic acid and 3-pyrrolidin-1-yl-propylamine.

Example II-121: 3-[5-Amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-benzoic acid using the same procedures a 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid from 5-bromo-3-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-ylamine and 3-methoxycarbonylbenzeneboronic acid.

Example II-122: {3-[5-Amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone was prepared following procedure 4 starting from 3-[5-Amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-benzoic acid and 4-pyrrolidin-1-yl-piperidin-1-ylamine.

Example II-145: 4-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-benzoic acid was prepared using the same procedure as 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid from 5-bromo-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-ylamine and 4-methoxycarbonylbenzeneboronic acid.

Example II-148: 4-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-((R)-2-hydroxy-3-pyrrolidin-1-yl-propyl)-benzamide was prepared following procedure 4 starting from 4-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-benzoic acid and (R)-2-hydroxy-3-pyrrolidin-1-yl-propylamine.

Example II-156: 4-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-benzoic acid was prepared using the same procedure as 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid from 5-bromo-3-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-ylamine and 4-methoxycarbonylbenzeneboronic acid.

Example II-157: (4-{5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone was prepared following procedure 4 starting from 4-{5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-benzoic acid and 4-pyrrolidin-1-yl-piperidin-1-ylamine.

Example II-168: 3-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-benzoic acid was prepared using the same procedure as 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid from 5-bromo-3-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-ylamine and 3-methoxycarbonylbenzeneboronic acid.

Example II-189: 3-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(1-methyl-piperidin-4-yl)-benzamide was prepared following procedure 4 starting from 3-[5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-benzoic acid and 1-methyl-piperidin-4-ylamine.

Example II-193: 5-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophene-2-carboxylic acid was prepared following procedure 3 starting from 5-bromo-3-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-ylamine and 5-carboxythiophene-2-boronic acid.

Example II-194: {5-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophen-2-yl}-(4-methyl-piperazin-1-yl)-methanone was prepared following procedure 4 starting from 5-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophene-2-carboxylic acid and 4-methyl-piperazin-1-ylamine.

Examples L-1 to L-176 were prepared according to procedure 40. In Table 5, the compounds are grouped into sections, with each section having a letter designation. Example numbers are assigned left to right by rows. For example, in Section A, the compounds in the top row, from left to right, are Examples L-1 to L-4, and the compounds in the second row are, from left to right, Examples L-5-L-8. % Inhibition is the percent c-MET inhibition at 50nM.

Examples L-177 to L-352 were prepared according to procedure 41. In Table 6, the compounds are grouped into sections, with each section having a letter designation. Example numbers are assigned left to right by rows. % Inhibition is the percent c-MET inhibition at 1μM.

Examples L-353 to L-548 were prepared according to procedure 42. In Table 7, the compounds are grouped into sections, with each section having a letter designation. Example numbers are assigned left to right by rows. % Inhibition is the percent c-MET inhibition at 1 μM.

Examples L-549 to L-636 were prepared according to procedure 43. In Table 8, the compounds are grouped into sections, with each section having a letter designation. Example numbers are assigned left to right by rows. % Inhibition is the percent c-MET inhibition at 1 μM.

BIOLOGICAL EXAMPLES

It will be appreciated that, in any given series of compounds, a range of biological activities will be observed. In its presently preferred aspects, this invention relates to novel compounds capable of modulating, regulating and/or inhibiting protein kinase activity. The following assays may be employed to select those compounds demonstrating the optimal degree of the desired activity.

Assay Procedures

The following *in vitro* assay may be used to determine the level of activity and effect of the different compounds of the present invention on one or more of the PKs. Similar assays can be designed along the same lines for any PK using techniques well known in the art. A literature reference is provided (Technikova-Dobrova Z, Sardanelli AM, Papa S FEBS Lett. 1991 Nov 4; 292: 69-72).

The general procedure is as follows: compounds and kinase assay reagents are introduced into test wells. The assay is initiated by addition of the kinase enzyme. Enzyme inhibitors reduce the measured activity of the enzyme.

In the continuous-coupled spectrophotometric assay the time-dependent production of ADP by the kinase is determined by analysis of the rate of consumption of NADH by measurement of the decrease in absorbance at 340 nm. As the PK produces ADP it is re-converted to ATP by reaction with phosphoenol pyruvate and pyruvate kinase. Pyruvate is also produced in this reaction. Pyruvate is subsequently converted to lactate by reaction with lactate dehydrogenase, which simultaneously converts NADH to NAD. NADH has a measurable absorbance at 340 nm whereas NAD does not.

The presently preferred protocol for conducting the continuous-coupled spectrophotometric experiments for specific PKs is provided below. However, adaptation of this protocol for determining the activity of compounds against other RTKs, as well as for CTKs and STKs, is well within the scope of knowledge of those skilled in the art.

HGFR Continuous-coupled Spectrophotometric Assay

This assay analyzes the tyrosine kinase activity of HGFR on the Met-2 substrate peptide, a peptide derived from the activation loop of the HGFR.

Materials and Reagents:

1. HGFR enzyme from Upstate (Met, active) Cat. # 14-526
2. Met-2 Peptide (HGFR Activation Loop) Ac-ARDMYDKEYYSVHNK (MW = 1960). Dissolve up in 200 mM HEPES, pH 7.5 at 10 mM stock.
3. 1 M PEP (phospho-enol-pyruvate) in 200 mM HEPES, pH 7.5
4. 100 mM NADH (B-Nicotinamide Adenine Dinucleotide, Reduced Form) in 200mM HEPES, pH 7.5
5. 4 M $MgCl_2$ (Magnesium Chloride) in ddH_2O
6. 1 M DTT (Dithiothreitol) in 200 mM HEPES, pH 7.5
7. 15 Units/mL LDH (Lactic Dehydrogenase)
8. 15 Units/mL PK (Pyruvate Kinase)
9. 5M NaCl dissolved in ddH_2O
10. Tween-20 (Protein Grade) 10% Solution
11. 1 M HEPES buffer: (N-[2-Hydroxethyl]piperazine-N-[2-ethanesulfonic acid]) Sodium Salt. Dissolve in ddH2O, adjust pH to 7.5, bring volume to 1 L. Filter at 0.1 µm.
12. HPLC Grade Water; Burdick and Jackson #365-4, 1 X 4 liters (or equivalent)
13. 100% DMSO (SIGMA)
14. Costar # 3880 – black clear flat bottom half area plates for K_i determination and % inhibition
15. Costar # 3359 – 96 well polypropylene plates, round bottom for serial dilutions
16. Costar # 3635 – UV-plate clear flat bottom plates for % inhibition
17. Beckman DU-650 w/ micro cell holders
18. Beckman 4-position micro cell cuvette

Procedure:

Prep Dilution Buffer (DB) for Enzyme (For 30 mL prep)

1. DB final concentration is 2 mM DTT, 25 mM $NaCl_2$, 5 mM $MgCl_2$, 0.01% Tween-20, and 50 mM HEPES buffer, pH 7.5.
2. Make up 50 mM HEPES by adding 1.5 mL 1 M HEPES into 28.1 mL of ddH2O. Add rest of the reagents. Into 50 mL conical vial, add 60 uL of 1M DTT, 150 uL 5M $NaCl_2$, 150 uL 1M $MgCl_2$, and 30 uL of 10% Tween-20 to give total volume of 30 mL.
3. Vortex for 5-10 seconds
4. Aliquot out DB at 1 mL/tube and label tubes as "DB HGFR"
5. Note: This can be prepared and stored ahead of time.
6. Freeze un-used aliquots in microcentrifuge tubes at -20°C freezer.

Prep Compounds

1. For compound dilution plate, add 4 uL of 10 mM stock into column 1 of plate, and bring volume to 100 uL with 100% DMSO.
2. Set up the Precision 2000 dilution method. A final concentration of 200 uM compound in 50% DMSO, 100 mM HEPES (1:2 serial dilution).

Prep Coupled Enzymatic Buffer:

1. Final concentration in assay:

Reagent (Stock Conc.)	Final Conc. In Assay
a. PEP (1 M)	1 mM
b. NADH (100 mM)	300 uM
c. $MgCl_2$ (4 M)	20 mM
d. DTT (1 M)	2 mM
e. ATP (500 mM)	300 uM
f. HEPES 200 mM (pH 7.5)	100 mM
g. Pyruvate Kinase (PK)	15 units/mL
h. Lactic Dehydrogenase (LDH)	15 units/mL
i. Met-2 peptide (10 mM)	0.500 mM
j. HGFR	50 nM

2. For a 10 mL reaction buffer add 10 uL of 1M PEP, 33 uL of 100 mM NADH, 50 uL of 4M $MgCl_2$, 20 uL of 1M DTT, 6 uL of 500 mM ATP, and 500 uL of 10 mM Met-2 peptide into 100 mM HEPES buffer pH 7.5 and vortex/mix.
3. Add coupling enzymes, LDH and PK, into reaction mix. Mix by gentle inversion.

Running samples

1. Spectrophotometer seettings:
   - i. Absorbance wavelength (λ): 340 nm
   - ii. Incubation time: 10 min
   - iii. Run time: 10 min
   - iv. Temperature: 37°C
2. Add 85 µL of CE reaction mix into each well of assay plate.
3. Add 5 µL of diluted compound into a well of the assay plate.

4. Add 5 µL of 50% DMSO for negative control into last column of assay plate.
5. Mix with multi-channel pipettor or orbital shaker.
6. Pre-incubate for 10 minutes at 37°C.
7. Add 10 µL of 500 nM HGFR to each well of assay plate; the final HGFR concentration is 50 nM in a total final volume of 100 µL.
8. Measure activity for 10 minutes at λ = 340 nm and 37°C.

The following *in vitro* assays may be used to determine the level of activity and effect of the different compounds of the present invention on one or more of the PKs. Similar assays can be designed along the same lines for any PK using techniques well known in the art.

Several of the assays described herein are performed in an ELISA (Enzyme-Linked Immunosorbent Sandwich Assay) format (Voller, et al., 1980, "Enzyme-Linked Immunosorbent Assay," Manual of Clinical Immunology, 2d ed., Rose and Friedman, Am. Soc. Of Microbiology, Washington, D.C., pp. 359-371). General procedure is as follows: a compound is introduced to cells expressing the test kinase, either naturally or recombinantly, for a selected period of time after which, if the test kinase is a receptor, a ligand known to activate the receptor is added. The cells are lysed and the lysate is transferred to the wells of an ELISA plate previously coated with a specific antibody recognizing the substrate of the enzymatic phosphorylation reaction. Non-substrate components of the cell lysate are washed away and the amount of phosphorylation on the substrate is detected with an antibody specifically recognizing phosphotyrosine compared with control cells that were not contacted with a test compound.

The presently preferred protocols for conducting the ELISA experiments for specific PKs is provided below. However, adaptation of these protocols for determining the activity of compounds against other RTKs, as well as for CTKs and STKs, is well within the scope of knowledge of those skilled in the art.

Other assays described herein measure the amount of DNA made in response to activation of a test kinase, which is a general measure of a proliferative response. General procedure for this assay is as follows: a compound is introduced to cells expressing the test kinase, either naturally or recombinantly, for a selected period of time after which, if the test kinase is a receptor, a ligand known to activate the receptor is added. After incubation at least overnight, a DNA labeling reagent such as 5-bromodeoxyuridine (BrdU) or H^3-thymidine is added. The amount of labeled DNA is detected with either an anti-BrdU antibody or by measuring radioactivity and is compared to control cells not contacted with a test compound.

MET TRANSPHOSPHORYLATION ASSAY

This assay is used to measure phosphotyrosine levels on a poly(glutamic acid:tyrosine, 4:1) substrate as a means for identifying agonists/antagonists of met transphosphorylation of the substrate.

Materials and Reagents:

1. Corning 96-well ELISA plates, Corning Catalog # 25805-96.
2. Poly(glu-tyr), 4:1, Sigma, Cat. No; P 0275.
3. PBS, Gibco Catalog # 450-1300EB

4. 50 mM HEPES

5. Blocking Buffer: Dissolve 25 g Bovine Serum Albumin, Sigma Cat. No A-7888, in 500 mL PBS, filter through a 4 µm filter.

6. Purified GST fusion protein containing the Met kinase domain, SUGEN, Inc.

7. TBST Buffer.

8. 10% aqueous (MilliQue H_2O) DMSO.

9. 10 mM aqueous (dH_2O) Adenosine-5'-triphosphate, Sigma Cat. No. A-5394.

10. 2X Kinase Dilution Buffer: for 100 mL, mix 10 mL 1M HEPES at pH 7.5 with 0.4 mL 5% BSA/PBS, 0.2 mL 0.1 M sodium orthovanadate and 1 mL 5M sodium chloride in 88.4 mL dH_2O.

11. 4X ATP Reaction Mixture: for 10 mL, mix 0.4 mL 1 M manganese chloride and 0.02 mL 0.1 M ATP in 9.58 mL dH_2O.

12. 4X Negative Controls Mixture: for 10 mL, mix 0.4 mL 1 M manganese chloride in 9.6 mL dH_2O.

13. NUNC 96-well V bottom polypropylene plates, Applied Scientific Catalog # S-72092

14. 500 mM EDTA.

15. Antibody Dilution Buffer: for 100 mL, mix 10 mL 5% BSA/PBS, 0.5 mL 5% Carnation® Instant Milk in PBS and 0.1 mL 0.1 M sodium orthovanadate in 88.4 mL TBST.

16. Rabbit polyclonal antophosphotyrosine antibody, SUGEN, Inc.

17. Goat anti-rabbit horseradish peroxidase conjugated antibody, Biosource, Inc.

18. ABTS Solution: for 1 L, mix 19.21 g citric acid, 35.49 g Na_2HPO_4 and 500 mg ABTS with sufficient dH_2O to make 1 L.

19. ABTS/H_2O_2: mix 15 mL ABST solution with 2µL H_2O_2 five minutes before use.

20. 0.2 M HCl

Procedure:

1. Coat ELISA plates with 2 µg Poly(Glu-Tyr) in 100 µL PBS, hold overnight at 4 ° C.

2. Block plate with 150 µL of 5% BSA/PBS for 60 min.

3. Wash plate twice with PBS then once with 50 mM Hepes buffer pH 7.4.

4. Add 50 µl of the diluted kinase to all wells. (Purified kinase is diluted with Kinase Dilution Buffer. Final concentration should be 10 ng/well.)

5. Add 25 µL of the test compound (in 4% DMSO) or DMSO alone (4% in dH_2O) for controls to plate.

6. Incubate the kinase/compound mixture for 15 minutes.

7. Add 25 µL of 40 mM $MnCl_2$ to the negative control wells.

8. Add 25 µL ATP/ $MnCl_2$ mixture to the all other wells (except the negative controls). Incubate for 5 min.

9. Add 25 µL 500 mM EDTA to stop reaction.

10. Wash plate 3x with TBST.

11. Add 100 µL rabbit polyclonal anti-Ptyr diluted 1:10,000 in Antibody Dilution Buffer to each well. Incubate, with shaking, at room temperature for one hour.

12. Wash plate 3x with TBST.

13. Dilute Biosource HRP conjugated anti-rabbit antibody 1: 6,000 in Antibody Dilution buffer. Add 100 µL per well and incubate at room temperature, with shaking, for one hour.

14. Wash plate 1X with PBS.

15. Add 100 µl of ABTS/H_2O_2 solution to each well.

16. If necessary, stop the development reaction with the addition of 100 µl of 0.2M HCl per well.

17. Read plate on Dynatech MR7000 ELISA reader with the test filter at 410 nM and the reference filter at 630 nM.

BrdU INCORPORATION ASSAYS

The following assays use cells engineered to express a selected receptor and then evaluate the effect of a compound of interest on the activity of ligand-induced DNA synthesis by determining BrdU incorporation into the DNA.

The following materials, reagents and procedure are general to each of the following BrdU incorporation assays. Variances in specific assays are noted.

General Materials and Reagents:

1. The appropriate ligand.

2. The appropriate engineered cells.

3. BrdU Labeling Reagent: 10 mM, in PBS, pH7.4(Roche Molecular Biochemicals, Indianapolis, IN).

4. FixDenat: fixation solution (Roche Molecular Biochemicals, Indianapolis, IN).

5. Anti-BrdU-POD: mouse monoclonal antibody conjugated with peroxidase (Chemicon, Temecula, CA).

6. TMB Substrate Solution: tetramethylbenzidine (TMB, ready to use, Roche Molecular Biochemicals, Indianapolis, IN).

7. PBS Washing Solution : 1X PBS, pH 7.4.

8. Albumin, Bovine (BSA), fraction V powder (Sigma Chemical Co., USA).

General Procedure:

1. Cells are seeded at 8000 cells/well in 10% CS, 2mM Gln in DMEM, in a 96 well plate. Cells are incubated overnight at 37°C in 5% CO_2.

2. After 24 hours, the cells are washed with PBS, and then are serum-starved in serum free medium (0%CS DMEM with 0.1% BSA) for 24 hours.

3. On day 3, the appropriate ligand and the test compound are added to the cells simultaneously. The negative control wells receive serum free DMEM with 0.1% BSA only; the positive control cells receive the ligand but no test compound. Test compounds are prepared in serum free DMEM with ligand in a 96 well plate, and serially diluted for 7 test concentrations.

4. After 18 hours of ligand activation, diluted BrdU labeling reagent (1:100 in DMEM, 0.1% BSA) is added and the cells are incubated with BrdU (final concentration is 10 µM) for 1.5 hours.

5. After incubation with labeling reagent, the medium is removed by decanting and tapping the inverted plate on a paper towel. FixDenat solution is added (50 µl/well) and the plates are incubated at room temperature for 45 minutes on a plate shaker.

6. The FixDenat solution is removed by decanting and tapping the inverted plate on a paper towel. Milk is added (5% dehydrated milk in PBS, 200 µl/well) as a blocking solution and the plate is incubated for 30 minutes at room temperature on a plate shaker.

7. The blocking solution is removed by decanting and the wells are washed once with PBS. Anti-BrdU-POD solution is added (1:200 dilution in PBS, 1% BSA, 50 µl/well) and the plate is incubated for 90 minutes at room temperature on a plate shaker.

8. The antibody conjugate is removed by decanting and rinsing the wells 5 times with PBS, and the plate is dried by inverting and tapping on a paper towel.

9. TMB substrate solution is added (100 µl/well) and incubated for 20 minutes at room temperature on a plate shaker until color development is sufficient for photometric detection.

10. The absorbance of the samples are measured at 410 nm (in "dual wavelength" mode with a filter reading at 490 nm, as a reference wavelength) on a Dynatech ELISA plate reader.

HGF-Induced BrdU Incorporation Assay

Materials and Reagents:

1. Recombinant human HGF (Cat. No. 249-HG, R&D Systems, Inc. USA).

2. BxPC-3 cells (ATCC CRL-1687).

Remaining Materials and Reagents, as above.

Procedure:

1. Cells are seeded at 9000 cells/well in RPMI 10% FBS in a 96 well plate. Cells are incubated overnight at 37°C in 5% CO_2.

2. After 24 hours, the cells are washed with PBS, and then are serum starved in 100 µL serum-free medium (RPMI with 0.1% BSA) for 24 hours.

3. On day 3, 25 µL containing ligand (prepared at 1 µg/mL in RPMI with 0.1% BSA; final HGF conc. is 200 ng/mL) and test compounds are added to the cells. The negative control wells receive 25 µL serum-free RPMI with 0.1% BSA only; the positive control cells receive the ligand (HGF) but no test compound. Test compounds are prepared at 5 times their final concentration in serum-free RPMI with ligand in a 96 well plate, and serially diluted to give 7 test concentrations. Typically, the highest final concentration of test compound is 100 µM, and 1:3 dilutions are used (i.e. final test compound concentration range is 0.137-100 µM).

4. After 18 hours of ligand activation, 12.5 µL of diluted BrdU labeling reagent (1:100 in RPMI, 0.1% BSA) is added to each well and the cells are incubated with BrdU (final concentration is 10 µM) for 1 hour.

5. Same as General Procedure.

6. Same as General Procedure.

7. The blocking solution is removed by decanting and the wells are washed once with PBS. Anti-BrdU-POD solution (1:100 dilution in PBS, 1% BSA) is added (100 µL/well) and the plate is incubated for 90 minutes at room temperature on a plate shaker.

8. Same as General Procedure.

9. Same as General Procedure.

10. Same as General Procedure.

In Vivo Animal Models

XENOGRAFT ANIMAL MODELS

The ability of human tumors to grow as xenografts in athymic mice (*e.g.*, Balb/c, nu/nu) provides a useful in vivo model for studying the biological response to therapies for human tumors. Since the first successful xenotransplantation of human tumors into athymic mice, (Rygaard and Povlsen, 1969, Acta Pathol. Microbiol. Scand. 77:758-760), many different human tumor cell lines (*e.g.*, mammary, lung, genitourinary, gastro-intestinal, head and neck, glioblastoma, bone, and malignant melanomas) have been transplanted and successfully grown in nude mice. The following assays may be used to determine the level of activity, specificity and effect of the different compounds of the present invention. Three general types of assays are useful for evaluating compounds: cellular/catalytic, cellular/biological and in vivo. The object of the cellular/catalytic assays is to determine the effect of a compound on the ability of a TK to phosphorylate tyrosines on a known substrate in a cell. The object of the cellular/biological assays is to determine the effect of a compound on the biological response stimulated by a TK in a cell. The object of the in vivo assays is to determine the effect of a compound in an animal model of a particular disorder such as cancer.

Suitable cell lines for subcutaneous xenograft experiments include C6 cells (glioma, ATCC # CCL 107), A375 cells (melanoma, ATCC # CRL 1619), A431 cells (epidermoid carcinoma, ATCC # CRL 1555), Calu 6 cells (lung, ATCC # HTB 56), PC3 cells (prostate, ATCC # CRL 1435), SKOV3TP5 cells, S114 (NIH3T3 fibroblast cell line genetically engineered for cMet and HGF expressions from NCI), U-87MG (human malignant glioma, ATCC HTB 14) and NIH 3T3 fibroblasts genetically engineered to overexpress EGFR, PDGFR, IGF-1R or any other test kinase. The following protocol can be used to perform xenograft experiments:

Female athymic mice (BALB/c, nu/nu) are obtained from Simonsen Laboratories (Gilroy, CA). All animals are maintained under clean-room conditions in Micro-isolator cages with Alpha-dri bedding. They receive sterile rodent chow and water ad libitum.

Cell lines are grown in appropriate medium (for example, MEM, DMEM, Ham's F10, or Ham's F12 plus 5% - 10% fetal bovine serum (FBS) and 2 mM glutamine (GLN)). All cell culture media, glutamine, and fetal bovine serum are purchased from Gibco Life Technologies (Grand Island, NY) unless otherwise specified. All cells are grown in a humid atmosphere of 90-95% air and 5-10% CO_2 at 37°C. All cell lines are routinely subcultured twice a week and are negative for mycoplasma as determined by the Mycotect method (Gibco).

Cells are harvested at or near confluency with 0.05% Trypsin-EDTA and pelleted at 450 x g for 10 min. Pellets are resuspended in sterile PBS or media (without FBS) to a particular concentration and the cells are implanted into the hindflank of the mice (8 - 10 mice per group, 2 - 10 x 10^6 cells/animal). Tumor growth is measured over 3 to 6 weeks using venier callpers. Tumor volumes are calculated as a product of length x width x height unless otherwise indicated. P values are calculated using the Students t-test. Test compounds in 50 - 100 µL excipient (DMSO, or VPD:D5W) can be delivered by IP injection at different concentrations generally starting at day one after implantation.

Met Phosphorylation – Cellular Assay

Materials and Reagents:

1. Falcon 10 cm culture dishes.
2. A549 lung carcinoma cells.
3. F12K growth medium (with 2% FBS + 2mM glutamine.
4. F12K assay medium (with 0.1% BSA).
5. Fisher cell scrapers.
6. Lysis buffer (HNTG, 1 mM sodium orthovanidate, 1 mM PMSF and 2mM sodium fluoride).
7. 1.5 mL Eppendorf tubes.
8. Eppendorf microcentrifuge.
9. BCA assay reagents A and B (#23223 and 23224, Pierce).
10. Sample tube rotator.
11. Gel blot container rotator.
12. 5X sample buffer.
13. Novex pre-cast tris-glycine 8% acrylamide gels.
14. Bio-Rad electrophoresis chamber.
15. SDS-PAGE buffer.
16. TBS (pH 7.6) + 0.1% Triton X-100 (TBST), with and wihtout 5% milk.
17. Western blot transfer buffer.
18. Osmonics nitrocellulose paper.
19. Bio-Rad Transblot paper.
20. Gel transfer apparatus.
21. Anti-phosphotyrosine (mouse monoclonal).
22. Bio-Rad Kaleidoscope Prestained Standards (161-0324).
23. Anti-h-met (C-28) rabbit polyclonal, conjugated and non-conjugated with agarose (#sc-161 AC and sc-161, Santa Cruz Biotechnology, Inc.).
24. Donkey and anti-rabbit Ig-HRP (NA 934, Amersham).
25. Sheet anti-mouseIg-HRP (NA 931, Amersham).
26. SuperSignal West Pico Chemiluminescent Substrate (#34080, Pierce).
27. Saran Wrap.
28. Kodak BioMax exposure cassette.

29. Fuji X-ray film.

30. Kodak film developer.

Procedure:

1. Plate cells in 10 cm dishes with growth medium with 2% FBS + 2mM glutamine. Grow to near confluency.

2. Serum starve cells overnight in assay medium with 0.1% BSA.

3. Add drug to the plates, one dose per plate, usually in a 2-flod titration. Add assay medium (with the same DMSO concentration as the drugs) for no drug.

4. Incubate plates 4-5 hours with the drug, then add HG, 50 ng/mL for 10 minutes.

5. Wash plates once with PBS, add 400 µl lysis buffer, and scrape off the cells. Collect in 1.5 mL Eppendorf tubes.

6. After about 10-20 minutes in the lysis buffer, centrifuge lysates in a microcentrifuger at full speed (14,000g) and collect the supernatants in a separate Eppendorf tube.

7. Determine protein concentration with the BCA assay reagents.

8. Adjust sample concentration to 0.5 mg protein in 0.4 mL using lysis buffer.

9. Add 15 µl anti-h-met AC for immunoprecipitation, rotate samples for 2 hours at 4°C.

10. Wash samples 3 times with lysis buffer and resuspend in 35 µl 5X sample buffer.

11. Boil sample at 100°C for 10 minutes and microcentrifuge at highest setting for 30 minutes to pellet the agarose beads.

12. Load 15 µl each to 2 gels, one for anti-phosphorylation and the other for anti-h-met. Also load 10 µl of prestained standards, one lane per gel.

13. Run gel around 100-125 V, then transfer gel to nitrocellulose either overnight at 70 mAmps or 1 hour at 500 mAmps.

14. Block membranes on rotator for 1 hour in TBS + 0.1% Triton X-100 (TBST) + 5% PBS. All steps from this point are at room temperature unless otherwise unless otherwise noted.

15. Add 0.8 µg/mL antiphosphotyrosine and 0.25 µg/mL anti-h-met on rotator either for 2 hours or overnight.

16. Wash membranes 3 times 5 minutes each in TBST on rotator.

17. Add HRP-conjugated antibodies)sheep anti-mouse for the antiphosphotyroeins; donkey anti-rabbit for the nati-h-met) at 1:5000 for approximately 45 minutes on rotator.

18. Wash membranes 3 times for 5 minutes each in TBST on rotator.

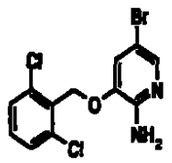
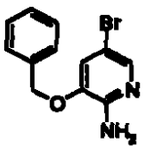
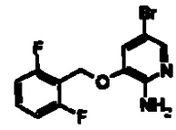
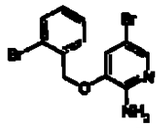
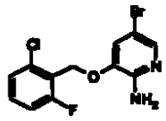
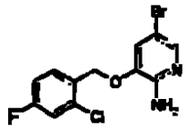
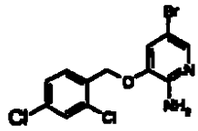
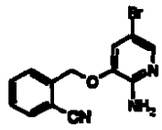
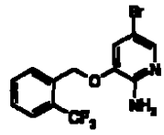
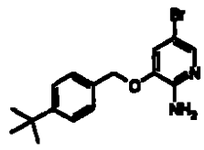
19. Add the 2 reagents in th3e SuperSignal kit together in equal volumes (3 mL + 3 mL for each blot), rotate for 1 –2 minutes.

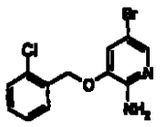
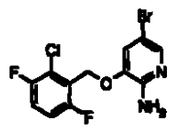
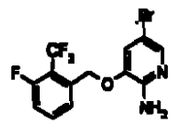
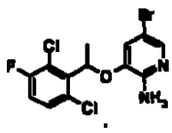
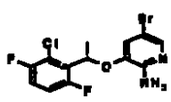
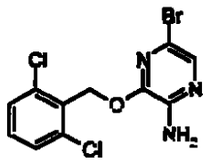
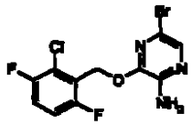
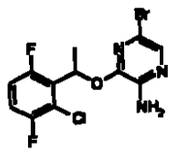
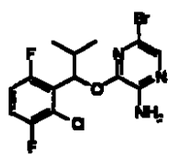
20. Wrap blots in Saran Wrap and tape securely inside the exposure cassette.

21. In the darkroom with only the safety light on, place a sheet of film inside the cassette. After an allotted time, remove film and place in the developer machine for automatic processing. Experiment with the exposure time to get proper exposure.

TABLES

Table 1

No.	Structure	Name	Met IC_{50} (μM)	^{1}H-NMR	MS m/z (M+1)
I(a)		5-Bromo-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine	5.3	(400 MHz, DMSO-d_6) δ 7.62 (m, 1H), 7.56 (m, 2H), 7.46 (m, 2H), 5.80 (s, 2H), 5.22 (s, 2H)	349
I(b)		3-Benzyloxy-5-bromo-pyridin-2-ylamine	>20	(400 MHz, DMSO-d_6) δ 7.56 (d, J = 2 Hz, 1H), 7.47 (d, J = 7.2 Hz, 2H), 7.38 (m, 2H), 7.32 (d, J = 7.2 Hz, 1H), 7.26 (d, J = 2 Hz, 1H), 5.95 (s, 2H), 5.14 (s, 2H)	280
I(c)		5-Bromo-3-(2,6-difluoro-benzyloxy)-pyridin-2-ylamine	40% at 20 μM	(400 MHz, DMSO-d_6) δ 7.60 (d, 1H), 7.52 (m, 1H), 7.40 (d, 1H), 7.18 (m, 2H), 5.81 (br. S. 2H), 5.12 (s, 2H)	315 (M+)
I(d)		5-Bromo-3-(2-bromo-benzyloxy)-pyridin-2-ylamine	>20	(400 MHz, DMSO-d_6) δ 7.85 (m, 2H), 7.80 (d, 1H), 7.42 (m, 2H), 7.30 (d, 1H), 5.84 (s 2H), 5.13 (s, 2H)	357 (M+)
I(e)		5-Bromo-3-(2-chloro-6-fluoro-benzyloxy)-pyridin-2-ylamine	>20	(400 MHz, DMSO-d_6) δ 7.80-7.30 (m, 5H), 5.80 (br s, 2H), 5.15 (s, 2H)	331
I(f)		5-Bromo-3-(2-chloro-4-fluoro-benzyloxy)-pyridin-2-ylamine		(400 MHz, DMSO-d_6) δ 7.80-7.20 (m, 5H), 5.95 (br s, 2H), 5.10 (s, 2H)	331
I(g)		5-Bromo-3-(2,4-dichloro-benzyloxy)-pyridin-2-ylamine		(400 MHz, DMSO-d_6) δ 7.80-7.50 (m, 5H), 6.20 (br s, 2H), 5.20 (s, 2H)	348
I(h)		2-(2-Amino-5-bromo-pyridin-3-yloxymethyl)-benzonitrile		(400 MHz, DMSO-d_6) δ 7.90-7.30 (m, 6H), 5.90 (br s, 2H), 5.20 (s, 2H)	304 (M+)
I(i)		5-Bromo-3-(2-trifluoromethyl-benzyloxy)-pyridin-2-ylamine		(400 MHz, DMSO-d_6) δ 7.80-7.30 (m, 6H), 6.00 (br s, 2H), 5.25 (s, 2H)	347
I(j)		5-Bromo-3-(4-*tert*-butyl-benzyloxy)-pyridin-2-ylamine		(400 MHz, DMSO-d_6) δ 7.50-7.20 (m, 6H), 5.85 (br s, 2H), 5.05 (s, 2H), 1.25 (s, 9H)	335 (M+)

No.	Structure	Name	Met IC_{50} (μM)	^{1}H-NMR	MS m/z (M+1)
I(k)		5-Bromo-3-(2-chloro-benzyloxy)-pyridin-2-ylamine		(400 MHz, DMSO-d_6) δ 7.70-7.20 (m, 6H), 5.90 (br s, 2H), 5.15 (s, 2H)	313
I(l)		5-Bromo-3-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-2-ylamine	5.3	($CDCl_3$, 300 MHz) δ 4.7-4.8 (brs, 2H), 5.21 (s, 2H), 7.03-7.10 (dt, 1H, J, 4.1, 9.1), 7.17-7.25 (m, 2H), 7.75-7.76 (d, J, 1.86).	
I(m)		5-Bromo-3-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-2-ylamine			365
I(n)		5-Bromo-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine		($CDCl_3$, 300 MHz) δ 1.85-1.95 (d, 3H), 4.7-5.0 (brs, 2H), 5.9-6.01 (q, 1H), 6.8-6.95 (d, 1H), 7.01-7.2 (t, 1H), 7.4-7.45 (m, 1H), 7.8-7.85 (d, 1H).	
I(o)		5-Bromo-3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-2-ylamine			364
II(a)		5-Bromo-3-(2,6-dichloro-benzyloxy)-pyrazin-2-ylamine	>20	(400 MHz, DMSO-d_6) δ 5.45 (s, 2H), 6.45 (s, 2H), 7.50 (m, 3H), 7.63 (s, 1H)	350
II(b)		5-Bromo-3-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-ylamine	>20	(300 MHz, $CDCl_3$) δ 7.7 (s, 1H), 7.23-7.16 (m, 1H), 7.09-7.01 (m, 1H), 5.53 (s, 2H), 4.72 (s, 2H)	351
II(c)		5-Bromo-3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-ylamine	1.81/ 2.67	(400 MHz, DMSO-d_6) δ 1.75 (d, 3H), 6.26 (m, 1H), 6.46 (s, 2H), 7.28 (m, 1H), 7.41 (m, 1H), 7.52 (s, 1H)	365
II(d)		5-Bromo-3-[1-(2-chloro-3,6-difluoro-phenyl)-2-methyl-propoxy]-pyrazin-2-ylamine	18.1	(400 MHz, DMSO-d_6) δ 0.92 (d, 3H), 1.17 (m, 3H), 2.57 (m, 1H), 5.75 (d, 1H), 6.49 (s, 2H), 7.24 (m, 1H), 7.40 (m, 1H), 7.54 (s, 1H)	393

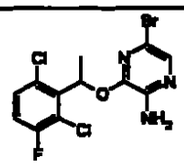
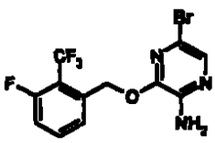
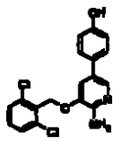
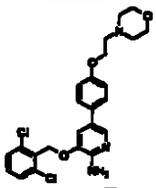
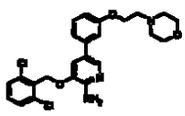
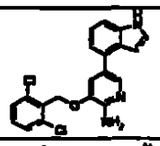
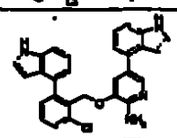
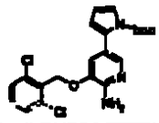
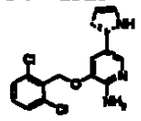
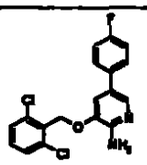
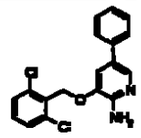
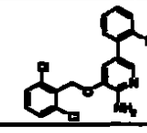
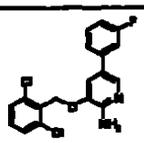
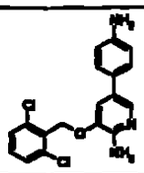
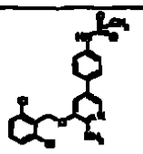
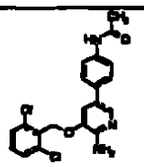
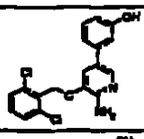
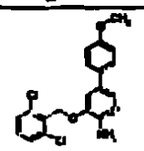
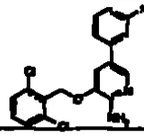
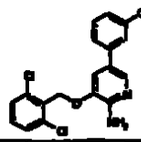
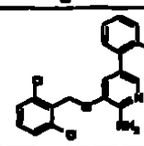
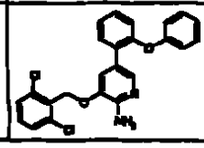
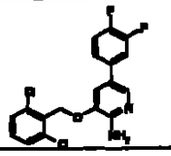
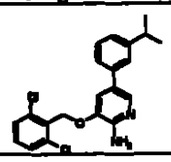
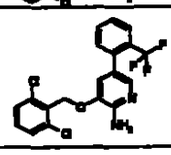
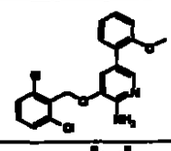
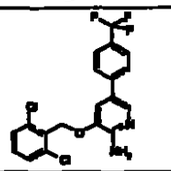
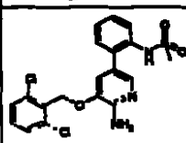
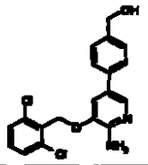
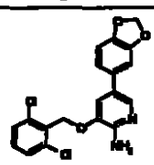
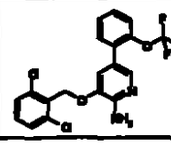
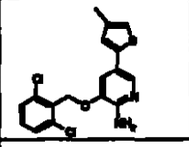
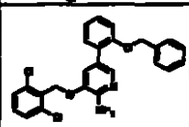
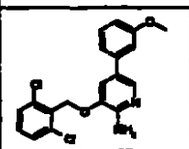
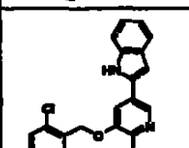
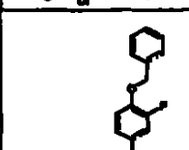
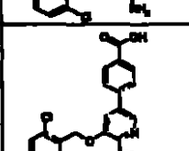
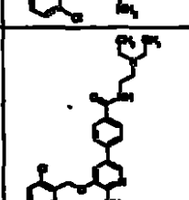
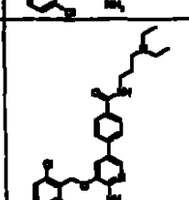
No.	Structure	Name	Met IC_{50} (μM)	^{1}H-NMR	MS m/z (M+1)
II(e)		5-Bromo-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-ylamine	0.24/ 0.68/ 1.3	(400 MHz, DMSO-d_6) δ 1.74 (d, 3H), 6.40 (m, 1H), 6.52 (br s, 2H), 7.30 (m, 1H), 7.48 (m, 1H), 7.56 (s, 1H); MS m/z 382 (M+1).	382
II(f)		5-Bromo-3-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-ylamine			366

Table 2

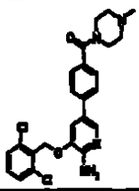
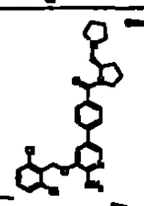
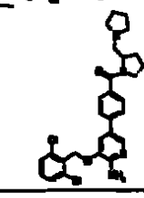
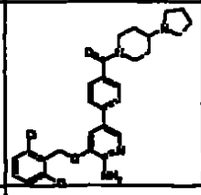
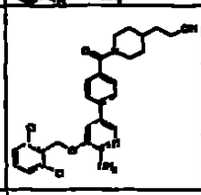
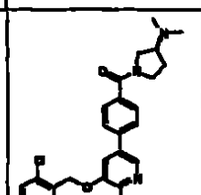
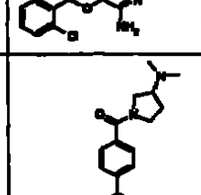
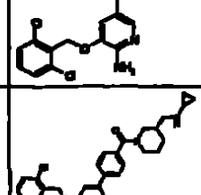
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-1		4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenol	0.279	see examples	(400 MHz, DMSO-d_6) δ 9.36 (s, 1H, OH), 7.77 (s, 1H), 7.54 (d, J = 8.2 Hz, 2H), 7.43 (m, 4H), 6.78 (d, J = 8.2 Hz, 2H), 5.49 (br. s, 2H, NH_2), 5.30 (s, 2H, CH_2).	362
I-2		3-(2,6-Dichloro-benzyloxy)-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine	0.56	see examples	(400 MHz, DMSO-d_6) δ 7.81 (d, J = 1.2 Hz, 1H), 7.53 (m, 3H), 7.48 (m, 3H), 6.97 (d, 2H), 5.53 (br. s, 2H, NH_2), 5.31 (s, 2H, CH_2), 4.08 (t, 2H), 3.58 (t, 4H), 2.68 (t, 2H), 2.48 (t, 4H).	374
I-3		3-(2,6-Dichloro-benzyloxy)-5-[3-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine	0.59	see examples	(400 MHz, DMSO-d_6) δ 7.89 (d, J = 1.2 Hz, 1H), 7.64 (d, J = 5.2 Hz, 2H), 7.61 (d, J = 1.2 Hz, 1H), 7.44 (dd, 1H), 7.28 (dd, 1H), 7.18 (m, 2H), 6.83 (dd, 1H), 5.65 (br. s, 2H), 5.33 (s, 2H), 4.12 (t, 2H), 3.55 (t, 6H), 2.68 (t, 2H), 2.46 (t, 2H)	475
I-4		3-(2,6-Dichloro-benzyloxy)-5-(1H-indol-4-yl)-pyridin-2-ylamine	1.4	see examples	(400 MHz, DMSO-d_6) δ 11.18 (s, 1H, NH), 7.87 (d, 1H), 7.5 (d, 2H), 7.46 (d, 2H), 7.36 (m, 1H), 7.33 (m, 1H), 7.12 (t, 1H), 7.03 (d, 1H), 6.49 (d, 1H), 5.81 (br. s, 2H, NH_2), 5.31 (s, 2H, CH_2).	384
I-5		3-[2-Chloro-6-(1H-indol-4-yl)-benzyloxy]-5-(1H-indol-4-yl)-pyridin-2-ylamine	4.71	see examples		485
I-6		2-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-pyrrole-1-carboxylic acid tert-butyl ester	>20	see examples		435
I-7		3-(2,6-Dichloro-benzyloxy)-5-(1H-pyrrol-2-yl)-pyridin-2-ylamine	4.25	see examples	(400 MHz, DMSO-d_6) δ 11.05 (s, 1H), 7.85 (s, 1H), 7.58 (s, 1H), 7.55 (s, 1H), 7.50 (m, 2H), 6.75 (s, 1H), 6.35 (s, 1H), 6.05 (s, 1H), 5.60 (br. s, 2H), 5.30 (s, 2H).	335
I-8		3-(2,6-Dichloro-benzyloxy)-5-(4-fluoro-phenyl)-pyridin-2-ylamine	8.01	see examples	(400 MHz, DMSO-d_6) δ 7.89 (s, 1H), 7.69 (m, 2H), 7.58 (m, 3H), 7.48 (m, 1H), 7.23 (m, 2H), 5.70 (br. s, 2H), 5.35 (s, 2H).	364
I-9		3-(2,6-Dichloro-benzyloxy)-5-phenyl-pyridin-2-ylamine	3.9	see examples	(400 MHz, DMSO-d_6) δ 7.89 (d, J = 2 Hz, 1H), 7.83 (d, J = 8.8 Hz, 2H), 7.57 (d, J = 2 Hz, 1H), 7.54 (m, 2H), 7.43 (m, 1H), 7.40 (m, 2H), 7.26 (m, 1H), 5.68 (br. s, 2H), 5.34 (s, 2H).	345
I-10		3-(2,6-Dichloro-benzyloxy)-5-(2-fluoro-phenyl)-pyridin-2-ylamine	6.09	see examples	(400 MHz, DMSO-d_6) δ 7.78 (d, 1H), 7.55 (m, 2H), 7.54 (m 1H), 7.48 (m, 2H), 7.32 (m, 1H), 7.25 (m, 2H), 5.78 (br. s, 2H), 5.28 (s, 2H).	364

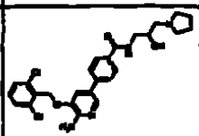
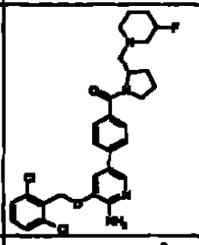
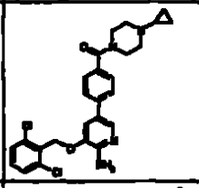
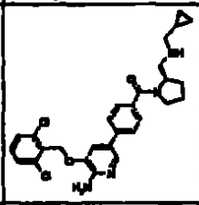
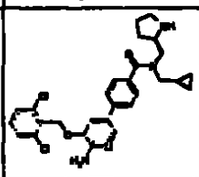
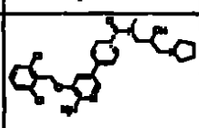
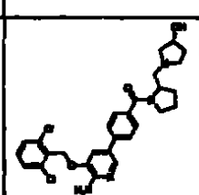
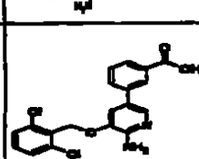
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-11		3-(2,6-Dichloro-benzyloxy)-6-(3-fluoro-phenyl)-pyridin-2-ylamine	13.8	see examples	(400 MHz, DMSO-d_6) δ 7.95 (d, 1H), 7.58-7.44 (m, 7H), 7.17 (m 1H), 6.78 (br. s, 2H), 5.35 (s, 2H).	364
I-12		5-(4-Amino-phenyl)-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine	0.908	see examples	(400 MHz, DMSO-d_6) δ 7.75 (d, 1H), 7.54 (dd, 4H), 7.47 (m, 1H), 7.40 (d, 1H), 7.29 (dd, 2H), 6.80 (dd, 2H), 5.44 (br. s, 2H), 5.31 (s, 2H), 5.18 (br s, 2H).	360
I-13		*N*-[4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl]-methanesulfonamide	0.44	see examples	(400 MHz, DMSO-d_6) δ 9.70 (s, 1H), 7.88 (d, 1H), 7.69 (m, 1H), 7.56 (m, 2H), 7.55 (m, 1H), 7.45 (m, 2H), 7.22 (dd, 2H), 5.63 (br. s, 2H), 5.33 (s, 2H), 2.95 (s, 3H).	439
I-14		N-[4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl]-acetamide	>20	see examples	(400 MHz, DMSO-d_6) δ 9.94 (s, 1H), 7.88 (d, 1H), 7.59 (m, 1H), 7.57 (m, 2H), 7.54 (m, 2H), 7.48 (m, 2H), 5.81 (br. s, 2H), 5.33 (s, 2H), 2.04 (s, 3H).	402
I-15		3-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenol	1.34	see examples	(400 MHz, DMSO-d_6) δ 7.53 (s, 1H), 7.55 (dd, 2H), 7.46 (m 2H), 7.19 (m, 1H), 7.10 (m, 1H), 7.04 (m, 1H), 6.95 (m, 1H), 6.69 (m, 1H), 5.67 (br. s, 2H), 5.33 (s, 2H).	360
I-16		3-(2,6-Dichloro-benzyloxy)-5-(4-methoxy-phenyl)-pyridin-2-ylamine	6.65	see examples	(400 MHz, DMSO-d_6) δ 7.83 (s, 1H), 7.82-7.54 (m, 4H), 6.97 (dd, 2H), 6.66 (dd, 2H), 5.59 (br. s, 2H), 5.33 (s, 2H), 3.77 (s, 3H).	357
I-17		5-(3-Amino-phenyl)-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine	1.07	see examples	(300 MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.66 (m, 1H), 7.45 (m, 1H), 7.38 (t, 1H), 7.28 (d, 1H), 7.22 (m, 1H), 6.93 (d, 1H), 6.86 (d, 1H), 6.64 (dd, 1H), 5.34 (s, 2H), 4.73 (br s, 2H), 4.12 (br s, 2H).	360
I-18		3-(2,6-Dichloro-benzyloxy)-5-(3-trifluoromethoxy-phenyl)-pyridin-2-ylamine	>20	see examples	(300 MHz, $CDCl_3$) δ 7.95 (d, 1H), 7.49-7.24 (m, 7H), 7.17 (m, 1H), 5.39 (s, 2H), 4.81 (br s, 2H).	429
I-19		2-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenol	2.16	see examples	(300 MHz, $CDCl_3$) δ 7.81 (d, 1H), 7.56 (m, 2H), 7.52 (m, 1H), 7.37 (d, 1H), 7.28 (m, 3H), 6.99 (m, 2H), 5.32 (s, 2H), 4.77 (br s, 2H)	381
I-20		3-(2,6-Dichloro-benzyloxy)-5-(2-phenoxy-phenyl)-pyridin-2-ylamine	>20	see examples	(300 MHz, $CDCl_3$) δ 7.88 (d, 1H), 7.69 (m, 2H), 7.45 (m, 3H), 7.34 (m, 2H), 7.28 (m, 3H), 7.07 (m, 2H), 6.93 (, 2H), 5.16 (s, 2H), 4.66 (br s, 2H).	437

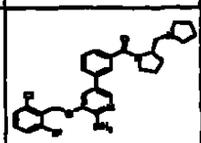
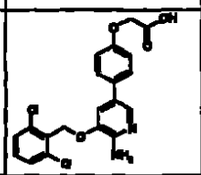
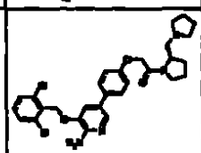
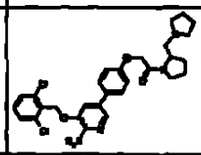
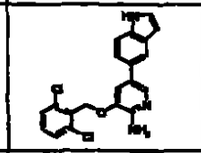
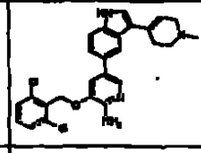
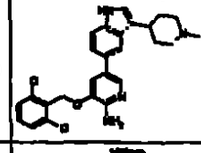
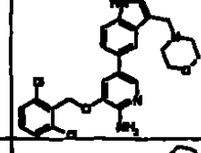
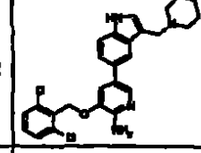
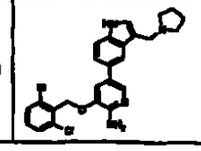
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS *m/z* (M+1)
I-21		3-(2,6-Dichloro-benzyloxy)-5-(3,4-difluoro-phenyl)-pyridin-2-ylamine	14.3	see examples	(300 MHz, $CDCl_3$) δ 7.89 (d, 1H), 7.40 (d, 2H), 7.26 (m, 5H), 5.37 (s, 2H), 4.60 (br s, 2H).	381
I-22		3-(2,6-Dichloro-benzyloxy)-5-(3-isopropyl-phenyl)-pyridin-2-ylamine	16.9	see examples	(300 MHz, $CDCl_3$) δ 7.86 (d, 1H), 7.40-7.15 (m, 6H), 5.38 (s, 2H), 4.73 (br s, 2H), 2.98 (m, 1H), 1.31 (d, 6H).	387
I-23		3-(2,6-Dichloro-benzyloxy)-5-(2-trifluoromethyl-phenyl)-pyridin-2-ylamine	>20	see examples	(300 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.7 Hz, 1H), 7.69 (s, 1H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.47 (t, *J* = 7.4 Hz, 1H), 7.36 (d, *J* = 7.4 Hz, 2H), 7.27 (m, 2H), 7.17 (s, 1H), 5.29 (s, 2H), 4.78 (br s, 2H).	413
I-24		3-(2,6-Dichloro-benzyloxy)-5-(2-methoxy-phenyl)-pyridin-2-ylamine	11.5	see examples	(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.41-7.24 (m, 6H), 7.02 (m, 2H), 5.32 (s, 2H), 4.69 (br s, 2H), 3.84 (s, 3H).	375
I-25		3-(2,6-Dichloro-benzyloxy)-5-(4-trifluoromethyl-phenyl)-pyridin-2-ylamine	>20	see examples	(300 MHz, $CDCl_3$) δ 7.86 (d, *J* = 1.8 Hz, 1H), 7.66 (m, 3H), 7.36 (m, 3H), 7.29 (m, 2H), 7.69 (s, 1H), 5.38 (s, 2H), 4.93 (br s, 2H)	413
I-26		*N*-[2-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl]-methanesulfonamide	>20	see examples	(300 MHz, $CDCl_3$) δ 8.75 (br s, 1H), 7.70-7.14 (m, 9H), 6.31 (s, 2H), 5.19 (br s, 2H), 3.18 (s, 3H)	438
I-27		[4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl]-methanol	2.6	see examples	(300 MHz, $CDCl_3$) δ 7.84 (d, *J* = 1.8 Hz,1H), 7.66 (m, 2H), 7.43-7.18 (m, 6H), 5.36 (s, 2H), 4.75 (d, 2H), 4.73 (br s, 2H), 2.6 (br, 1H)	375
I-28		5-Benzo[1,3]dioxol-5-yl-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine	8.6	see examples	(300 MHz, $CDCl_3$) δ 7.88 (d, *J* = 1.5 Hz,1H), 7.37 (m, 2H), 7.29 (m, 2H), 6.99 (d, 2H), 6.87 (d, 1H), 6.09 (s, 2H), 5.36 (s, 2H), 4.74 (br s, 2H)	389
I-29		3-(2,6-Dichloro-benzyloxy)-5-(2-trifluoromethoxy-phenyl)-pyridin-2-ylamine	>20	see examples	(300 MHz, $CDCl_3$) δ 7.82 (s,1H), 7.47-7.25 (m, 8H), 5.33 (s, 2H), 4.82 (br s, 2H)	429

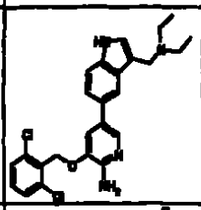
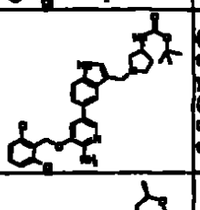
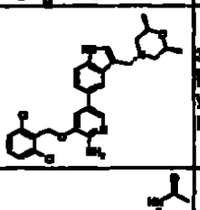
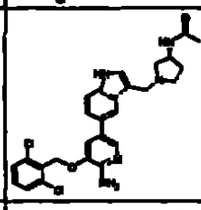
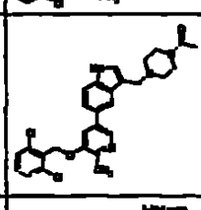
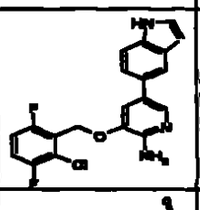
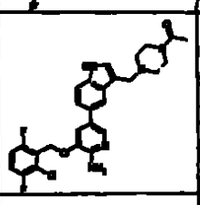
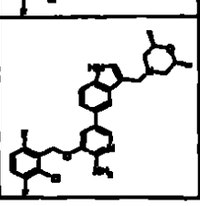
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-30		3-(2,6-Dichloro-benzyloxy)-5-(4-methyl-thiophen-2-yl)-pyridin-2-ylamine	3.6	see examples	(300 MHz, $CDCl_3$) δ 7.98 (d, J = 1.9 Hz, 1H), 7.37 d, J = 8.5 Hz, 2H), 7.29 (m, 2H), 7.00 (d, J = 1.1 Hz, 1H), 6.80 (s, 1H), 5.34 (s, 2H), 4.80 (br s, 2H), 2.28 (s, 3H)	365
I-31		5-(2-Benzyloxy-phenyl)-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine	>20	see examples	(300 MHz, $CDCl_3$) δ 7.90 (d, J = 1.7 Hz, 1H), 7.49 (d, J = 1.7 Hz, 1H), 7.31 (m, 10H), 7.06 (m, 2H), 5.06 (s, 2H), 4.77 (br s, 2H).	451
I-32		3-(2,6-Dichloro-benzyloxy)-5-(3-methoxy-phenyl)-pyridin-2-ylamine	4.81	see examples	(300 MHz, $CDCl_3$) δ 7.98 (d, J = 1.7 Hz, 1H), 7.39-7.11 (m, 4H), 7.13 (d, J = 7.7 Hz, 2H), 7.07 (t, J = 2.1 Hz, 1H), 6.89 (dd, J = 8.2 Hz, 2.1 Hz, 1H), 5.36 (s, 2H), 4.79 (br s, 2H), 3.87 (s, 3H).	375
I-33		3-(2,6-Dichloro-benzyloxy)-5-(1*H*-indol-2-yl)-pyridin-2-ylamine	7.5	see examples	(300 MHz, $CDCl_3$) δ 8.47 (br s, 1H), 8.04 (s, 1H), 7.70 (d, J = 8.5 Hz, 1H), 7.62-7.11 (m, 6H), 6.71 (d, J = 1.3 Hz, 1H), 5.69 (dd, J = 7.7 Hz, 2.1 Hz, 1H), 5.29 (s, 2H), 4.73 (br s, 2H).	384
I-34		5-(4-Benzyloxy-3-fluoro-phenyl)-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine	13.5	see examples	(400 MHz, DMSO-d_6) δ 5.20 (s, 2H), 5.32 (s, 2H), 5.85 (s, 2H), 7.25 (t, 1H), 7.33 (m, 1H), 7.39 (m, 3H), 7.46 (m, 3H), 7.51 (m, 4H), 7.66 (s, 1H)	469
I-35		4-[5-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid	12.9	see examples	(400 MHz, DMSO-d_6) δ 7.98 (s, 1H), 7.92 (d, J = 5.6 Hz, 2H), 7.75 (d, J = 4.8 Hz, 2H), 7.55 (d, J = 5.2 Hz, 1H), 7.54 (dd, 2H), 7.45 (m, 1H), 5.5 (br. s, 2H), 5.34 (s, 2H).	360
I-36		4-[5-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-N-(2-diethylamino-ethyl)-benzamide	0.99	see examples	(400 MHz, DMSO-d_6) δ 8.45 (s, 1H), 7.97 (d, J = 1.2 Hz, 1H), 7.86 (d, J = 5.6 Hz, 2H), 7.73 (d, J = 5.6 Hz, 2H), 7.60 (d, J = 1.2 Hz, 1H), 7.54 (d, J = 5.2 Hz, 2H), 7.44 (dd, 1H), 5.77 (br. s, 2H), 5.34 (s, 2H), 3.3 (m, 4H), 2.8 (m, 4H), 0.99 (t, 6H)	487
I-37		4-[5-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-N-(3-diethylamino-propyl)-benzamide	0.82	see examples	(400 MHz, DMSO-d_6) δ 8.60 (s, 1H), 7.95 (d, J = 1.2 Hz, 1H), 7.85 (d, J = 5.6 Hz, 1H), 7.76 (d, J = 5.6 Hz, 1H), 7.70 (d, J = 1.2 Hz, 1H), 7.60 (m, 1H), 7.55 (m, 2H), 7.45 (m, 2H), 5.70 (br. s, 2H), 5.36 (s, 2H), 3.3 (m, 4H), 2.8 (m, 4H), 1.7 (m, 2H), 1.0 (t, 6H)	501

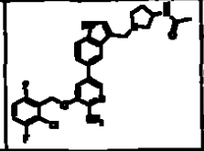
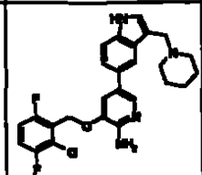
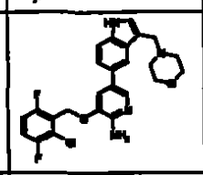
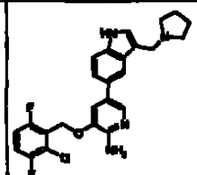
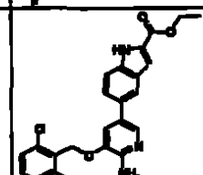
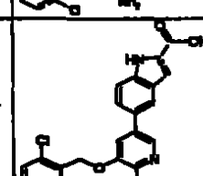
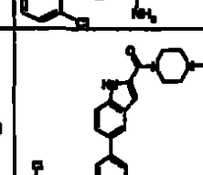
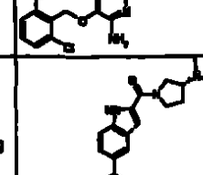
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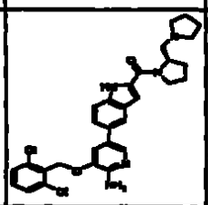
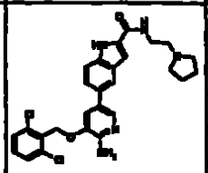
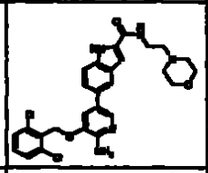
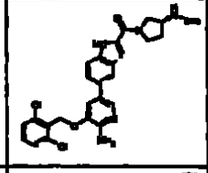
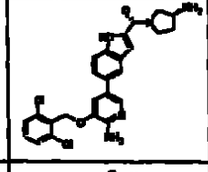
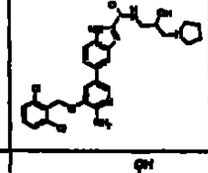
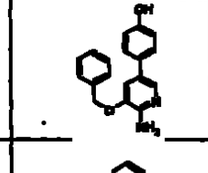
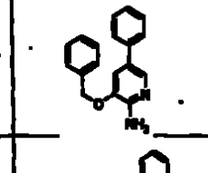
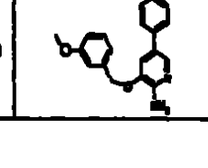
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS *m/z* (M+1)
I-38		{4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone	1.02	see examples	(400 MHz, DMSO-d_6) δ 7.95 (d, *J* = 2 Hz, 1H), 7.72 (dd, *J* = 6, 1.8 Hz, 2H), 7.59 (d, *J* = 1.8 Hz, 1H), 7.57 (d, *J* = 1.2 Hz, 1H), 7.55 (s, 1H), 7.43 (dd, *J* = 6, 1.2 Hz, 1H), 7.40 (dd, *J* = 6, 1.8 Hz, 2H), 5.76 (br. s, 2H), 5.35 (s, 2H), 3.6 (m, 4H), 2.3 (m, 4H), 2.2 (s, 3H).	471
I-39		{4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.082/ 0.11/ 0.2 (Ki 0.04)	see examples	(400 MHz, DMSO-d_6) δ 7.96 (d, 1H), 7.72 (dd, 2H), 7.69 (m, 2H), 7.54 (m, 2H), 7.47 (m, 2H), 5.76 (br. s, 2H), 5.36 (s, 2H), 4.35 (m, 1H), 3.5 (d, 2H), 3.0 (m, 4H), 1.7-2.0 (m, 10H).	525
I-40		{4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.21	see examples	(400 MHz, DMSO-d_6) δ 7.93 (d, 1H), 7.69 (dd, 2H), 7.57 (d, 1H), 7.54 (dd, 2H), 7.47 (m, 2H), 7.44 (m, 1H), 5.74 (br. s, 2H), 5.34 (s, 2H), 3.45 (m, 1H), 3.3 (m, 4H), 2.46 (m, 2H), 1.95 (m, 2H), 1.84 (m, 4H), 1.63 (m, 4H).	525
I-41		{4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-(1-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.35	see examples	(400 MHz, DMSO-d_6) δ 7.95 (d, 1H), 7.70 (dd, 2H), 7.65 (d, 1H), 7.48 (dd, 2H), 7.41 (m, 1H), 7.39 (m, 2H), 5.76 (br. s, 2H), 5.35 (s, 2H), 3.0 (m, 4H), 2.6 (m, 4H), 2.25 (s, 1H), 1.89 (m, 4H), 1.66 (m, 4H)	525
I-42		{4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[1-(2-hydroxy-ethyl)-piperidin-1-yl]-methanone	0.56	see examples	(400 MHz, DMSO-d_6) δ 7.94 (d, 1H), 7.71 (dd, 2H), 7.70 (d, 1H), 7.59 (dd, 2H), 7.55 (m, 1H), 7.45 (m, 2H), 5.76 (br. s, 2H), 5.35 (s, 2H), 4.35 (t, 2H), 3.60 (m, 1H), 3.44 (m, 2H), 3.0 (m, 2H), 1.66 (m, 2H), 1.40 (m, 2H), 1.37 (m, 2H)	500
I-43		{4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone	0.47	see examples	(400 MHz, DMSO-d_6) δ 7.95 (d, 1H), 7.75 (dd, 2H), 7.57 (d, 1H), 7.55 (dd, 2H), 7.48 (m, 1H), 7.46 (m, 2H), 5.76 (br. s, 2H), 5.35 (s, 2H), 3.60 (m, 1H), 3.0 (m, 2H), 2.2 (s, 3H), 2.1 (s, 3H), 1.15 (m, 2H)	485
I-44		{4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*R*)-3-dimethylamino-pyrrolidin-1-yl]-methanone	0.66	see examples	(400 MHz, DMSO-d_6) δ 7.95 (m, 1H), 7.72 (m, 2H), 7.60 (m, 1H), 7.55 (m, 2H), 7.48 (m, 3H), 5.76 (br. s, 2H), 5.35 (s, 2H), 3.50 (m, 3H), 3.0 (m, 2H), 2.1 (s, 3H), 2.05 (s, 3H), 1.1 (m, 2H)	485
I-45		{4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-3-cyclopropylaminomethyl-piperidin-1-yl]-methanone	0.77	see examples	(400 MHz, DMSO-d_6) δ 7.94 (d, 1H), 7.77 (m, 2H), 7.57 (m, 2H), 7.55 (m, 1H), 7.48 (dd, 1H), 7.39 (m, 2H), 5.79 (s, 2H), 5.35 (s, 2H), 4.4 (m, 1H), 3.6 (m, 1H), 2.6-3.0 (m, 4H), 1.4-1.8 (m, 8H), 0.8 (m, 2H).	528

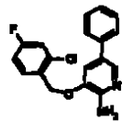
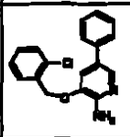
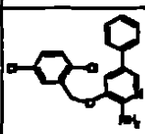
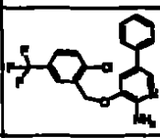
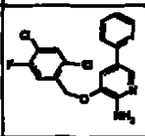
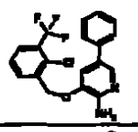
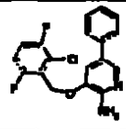
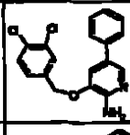
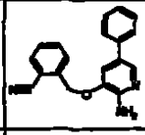
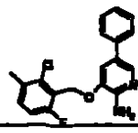
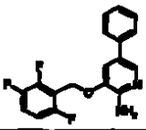
No.	Structure	Name	Met IC_{50} (nM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-46		4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-*N*-(2-hydroxy-3-pyrrolidin-1-yl-propyl)-benzamide	0.2	see examples	(400 MHz, DMSO-d_6) δ 8.49 (m, 1H), 7.99 (d, 2H), 7.86 (m, 2H), 7.75 (m, 2H), 7.61 (d, 1H), 7.57 (m, 2H), 7.46 (dd, 1H), 5.79 (s, 2H), 6.36 (s, 2H), 4.8 (m, 1H), 3.75 (m, 1H), 3.44 (m, 1H), 3.16 (m, 1H), 2.53 (m, 4H), 2.40 (m, 1H), 1.67 (m, 4H)	516
I-47		(4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl)-[(2*S*)-2-(3-fluoro-piperidin-1-ylmethyl)-pyrrolidin-1-yl]-methanone	0.42	see examples		657
I-48		(4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl)-(4-cyclopropyl-piperazin-1-yl)-methanone	1.67	see examples		497
I-49		(4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl)-[(2*R*)-2-[(cyclopropylmethyl-amino)-methyl]-pyrrolidin-1-yl]-methanone	0.57	see examples	(400 MHz, DMSO-d_6) δ 7.92 (d, 1H), 7.57 (m, 2H), 7.54 (m, 2H), 7.49 (m, 2H), 7.43 (m, 2H), 6.73 (s, 2H), 6.32 (s, 2H), 4.2 (m, 1H), 3.5 (m, 1H), 3.28 (m, 4H), 2.0-1.7 (m, 6H), 1.16 (m, 4H)	525
I-50		4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-N-cyclopropylmethyl-*N*-(2*R*)-pyrrolidin-2-ylmethyl-benzamide	0.29	see examples	(400 MHz, DMSO-d_6) δ 8.16 (d, 1H), 7.81 (d, 1H), 7.38 (m, 2H), 7.23-7.16 (m, 4H), 7.09 (m, 1H), 6.44 (s, 2H), 4.98 (s, 2H), 4.05 (m, 1H), 3.2 (m, 1H), 3.1 (m, 1H), 2.93 (m, 6H), 2.78 (m, 2H), 2.10 (m, 4H)	525
I-51		4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-N-(2-hydroxy-3-pyrrolidin-1-yl-propyl)-N-methyl-benzamide	0.71	see examples	(400 MHz, DMSO-d_6) δ 7.90 (m, 1H), 7.76 (m, 1H), 7.63 (m, 2H), 7.52 (d, 2H), 7.50 (m, 2H), 7.40 (m, 1H), 6.59 (s, 2H), 6.30 (s, 2H), 3.70 (m, 1H), 2.98 (s, 3H), 2.44 (m, 4H), 2.34 (m, 4H), 1.75 (m, 4H).	529
I-52		(4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl)-[(2*S*)-2-[(3*R*)-3-hydroxy-pyrrolidin-1-ylmethyl]-pyrrolidin-1-yl]-methanone	0.83	see examples	(400 MHz, DMSO-d_6) δ 7.99 (d, 1H), 7.70 (m, 2H), 7.60 (m, 1H), 7.57 (m, 1H), 7.55 (m, 3H), 7.46 (m, 1H), 6.76 (s, 2H), 5.37 (s, 2H), 4.3 (m, 1H), 3.6 (m, 4H), 3.2 (m, 4H), 1.9 (m, 4H), 1.24 (m, 4H).	541
I-53		3-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid	16	see examples	(400MHz, DMSO-d_6) δ 8.13 (m, 1H), 7.91 (d, 1H), 7.88(m, 2H), 7.58(dd, 2H), 7.54(m, 2H), 7.47(m, 1H),6.78(s, 2H), 5.36(s, 2H)	389

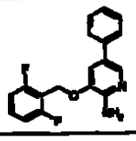
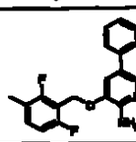
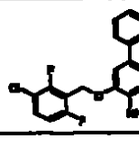
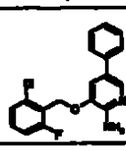
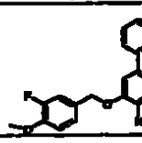
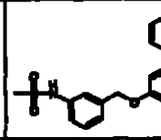
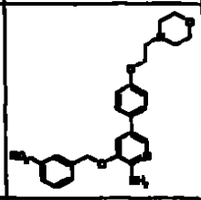
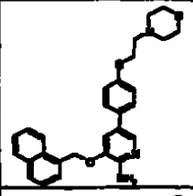
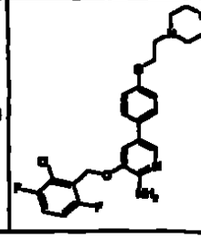
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-54		(3-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl)-[(2R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	2.5	see examples	(400MHz, DMSO-d_6) δ 7.93 (d, 1H), 7.74 (m, 2H), 7.56 (m, 3H), 7.48 (m, 2H), 7.38 (m, 1H), 5.74 (s, 2H), 5.35 (s,2H), 4.40 (m, 1H), 3.40 (d, 2H), 3.0 (m, 4H), 1.7-2.0 (m, 10H)	525
I-55		(4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenoxy)-acetic acid	2.41	see examples	(400 MHz, DMSO-d_6) δ 7.81 (d, 1H), 7.56 (m, 2H), 7.48 (m, 4H), 6.87 (m, 2H), 6.63 (s, 2H), 5.32 (s, 2H), 4.33 (s, 2H)	419
I-56		2-[4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenoxy]-1-[(2R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-ethanone	0.63	see examples	(400 MHz, DMSO-d_6) δ 7.77 (d, 1H), 7.52 (d, 1H), 7.47 (m, 3H), 7.41 (m, 2H), 6.88 (m, 2H), 5.51 (s, 2H), 5.28 (s, 2H), 4.57 (s, 2H), 4.20 (m, 1H), 3.42 (m, 2H), 1.82 (m, 4H), 1.66 (m, 10H).	555
I-57		2-[4-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenoxy]-1-[(2S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-ethanone	0.8	see examples	(400 MHz, DMSO-d_6) δ 7.82 (d, 1H), 7.57 (d, 1H), 7.52 (m, 3H), 7.45 (m, 2H), 6.93 (m, 2H), 5.56 (s, 2H), 5.33 (s, 2H), 4.72 (s, 2H), 4.20 (m, 1H), 3.5 (m, 2H), 2.52 (m, 6H), 1.85 (m, 4H), 1.66 (m, 4H)	555
I-58		3-(2,6-Dichloro-benzyloxy)-5-(1H-indol-5-yl)-pyridin-2-ylamine	4.3	see examples	(400 MHz, DMSO-d_6) δ 11.05 (s, 1H, NH), 7.87 (d, 1H), 7.78 (m, 1H), 7.57 (m, 3H), 7.40-7.48 (m, 2H), 7.34 (m, 2H), 6.44 (m, 1H), 6.49 (br. s, 2H, NH_2), 5.36 (s, 2H, CH_2)	384
I-59		3-(2,6-Dichloro-benzyloxy)-5-[3-(1-methyl-1,2,3,6-tetrahydro-pyridin-4-yl)-1H-indol-5-yl]-pyridin-2-ylamine	1.57	see examples	(400 MHz, DMSO-d_6) δ 11.35 (d, 1H, NH), 7.95 (s, 1H), 7.89 (d, 1H), 7.85 (m, 4H), 7.46 (m, 2H), 7.39 (dd, 1H), 6.25 (m, 1H), 5.54 (br. s, 2H, NH_2), 5.37 (s, 2H, CH_2), 3.77 (m, 2H), 3.32 (m, 2H), 2.52 (m, 2H), 2.20 (s, 3H).	460
I-60		3-(2,6-Dichloro-benzyloxy)-5-[3-(1-methyl-piperidin-4-yl)-1*H*-indol-5-yl]-pyridin-2-ylamine	3.04	see examples	(400 MHz, DMSO-d_6) δ 10.9 (d, 1H, NH), 7.90 (d, 1H), 7.80 (s, 1H), 7.55 (m, 4H), 7.46 (m, 2H), 7.32 (dd, 1H), 5.50 (br. s, 2H, NH_2), 5.38 (s, 2H, CH_2), 3.32 (m, 2H), 3.02 (m, 2H), 2.90 (m, 1H), 2.67 (s, 3H), 2.10 (m, 2H), 1.96 (m, 2H).	481
I-61		3-(2,6-Dichloro-benzyloxy)-5-(3-morpholin-4-ylmethyl-1*H*-indol-5-yl)-pyridin-2-ylamine	1.19	see examples	(400 MHz, DMSO-d_6) δ 2.31 (m, 4H), 3.55 (m, 4H), 3.66 (s, 2H), 5.28 (s, 2H), 5.45 (s, 2H), 7.22 (s, 1H), 7.34 (m, 2H), 7.48 (m, 2H), 7.57 (m, 2H), 7.80 (s, 1H), 7.85 (s, 1H), 10.92 (br s, 1H)	483
I-62		3-(2,6-Dichloro-benzyloxy)-5-(3-piperidin-1-ylmethyl-1*H*-indol-5-yl)-pyridin-2-ylamine	1.41	see examples	(300 MHz, $CDCl_3$) δ 1.43 (m, 2H), 1.60 (m, 4H), 2.50 (m, 4H), 3.76 (s, 2H), 4.65 (br s, 2H), 5.40 (s, 2H), 7.18 (s, 1H), 7.27 (m, 1H), 7.38 (m, 6H), 7.67 (s, 1H), 8.01 (d, J = 1.7 Hz, 1H), 8.17 (br s, 1H)	481
I-63		3-(2,6-Dichloro-benzyloxy)-5-(3-pyrrolidin-1-ylmethyl-1*H*-indol-5-yl)-pyridin-2-ylamine	1.34	see examples	(300 MHz, $CDCl_3$) δ 1.79 (m, 4H), 2.62 (m, 4H), 3.88 (s, 2H), 4.64 (br s, 2H), 5.40 (s, 2H), 7.21 (d, J = 2.3 Hz, 1H), 7.26 (m, 1H), 7.38 (m, 6H), 7.64 (s, 1H), 8.01 (d, J = 1.8 Hz, 1H), 8.10 (br s, 1H)	467

No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-64		3-(2,6-Dichloro-benzyloxy)-6-(3-diethylaminomethyl-1H-indol-5-yl)-pyridin-2-ylamine	3.23	see examples	(300 MHz, $CDCl_3$) δ 1.13 (t, 6H), 2.64 (q, 4H), 3.68 (s, 2H), 4.66 (br s, 2H), 5.37 (s, 2H), 7.18 (d, J = 1.7 Hz, 1H), 7.28 (m, 1H), 7.37 (m, 5H), 7.66 (s, 1H), 8.00 (d, J = 1.7 Hz, 1H), 8.44 (br s, 1H)	469
I-65		(1-[6-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-3-ylmethyl]-(3*R*)-pyrrolidin-3-yl)-carbamic acid *tert*-butyl ester	6.3	see examples	(300 MHz, $CDCl_3$) δ 1.39 (s, 9H), 2.22 (m, 1H), 2.40 (m, 1H), 2.58 (m, 1H), 2.68 (m, 1H), 2.99 (m, 1H), 3.62 (d, 1H), 3.68 (d, 1H), 4.18 (m, 1H), 4.65 (br s, 2H), 4.81 (m, 1H), 5.41 (s, 2H), 7.17 (d, J = 2.1 Hz, 1H), 7.28 (m, 1H), 7.36 (m, 6H), 7.61 (s, 1H), 8.00 (d, J = 1.8 Hz, 1H), 8.09 (br s, 1H)	582
I-66		3-(2,6-Dichloro-benzyloxy)-6-[3-(2,6-dimethyl-morpholin-4-ylmethyl)-1*H*-indol-5-yl]-pyridin-2-ylamine	>20	see examples	(300 MHz, $CDCl_3$) δ 1.13 (d, J = 6.3 Hz, 6H), 1.80 (t, J = 10.7 Hz, 2H), 1.84 (br s, 1H), 2.84 (d, J = 10.5 Hz, 2H), 3.72 (m, 4H), 4.66 (br s, 2H), 5.38 (s, 2H), 7.18 (d, J = 2.2 Hz, 1H), 7.28 (m, 1H), 7.38 (m, 6H), 7.89 (s, 1H), 8.10 (d, J = 1.7 Hz, 1H), 8.32 (br s, 1H)	511
I-67		*N*-(1-[6-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-3-ylmethyl]-(3*R*)-pyrrolidin-3-yl)-acetamide	1.79	see examples	(300 MHz, $CDCl_3$) δ 1.88 (s, 3H), 2.31 (m, 2H), 2.69 (m, 1H), 2.70 (m, 1H), 2.99 (m, 1H), 3.62 (d, 1H), 3.90 (d, 1H), 4.42 (m, 1H), 4.66 (br s, 2H), 5.40 (s, 2H), 5.91 (m, 1H), 7.15 (d, J = 2.2 Hz, 1H), 7.28 (m, 3H), 7.38 (m, 5H), 7.82 (s, 1H), 8.00 (d, J = 1.8 Hz, 1H), 8.33 (br s, 1H)	524
I-68		1-(4-[5-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-3-ylmethyl]-piperazin-1-yl)-ethanone	2.15	see examples	(300 MHz, $CDCl_3$) δ 2.07 (s, 3H), 2.61 (m, 4H), 3.44 (m, 2H), 3.63 (m, 2H), 3.78 (s, 2H), 4.66 (br s, 2H), 5.40 (s, 2H), 7.17 (d, J = 2.2 Hz, 1H), 7.28 (m, 1H), 7.38 (m, 6H), 7.88 (s, 1H), 8.00 (d, J = 1.8 Hz, 1H), 8.34 (br s, 1H)	524
I-69		3-(2-Chloro-3,6-difluoro-benzyloxy)-6-(1*H*-indol-5-yl)-pyridin-2-ylamine		see examples		398
I-70		1-(4-[5-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-1*H*-indol-3-ylmethyl]-piperazin-1-yl)-ethanone	0.8	see examples	(300 MHz, $CDCl_3$) δ 2.08 (s, 3H), 2.49 (m, 4H), 3.48 (m, 2H), 3.61(m, 2H), 3.80 (s, 2H), 4.68 (s, 2H), 5.30(s, 2H), 7.02 (m, 1H), 7.20 (m, 2H), 7.41 (m, 3H), 7.69(s, 1H), 8.08 (s, 1H), 8.63 (s, 1H)	526
I-71		3-(2-Chloro-3,6-difluoro-benzyloxy)-6-[3-(2,6-dimethyl-morpholin-4-ylmethyl)-1*H*-indol-5-yl]-pyridin-2-ylamine	2.71	see examples	(300 MHz, $CDCl_3$) δ 1.37 (d, 6H), 1.82 (m, 2H), 2.95 (m, 2H), 3.67(m, 4H), 4.68 (s, 2H), 5.34 (s, 2H), 7.08 (m, 1H), 7.27 (m, 2H), 7.48 (m, 3H), 7.89(s, 1H), 7.98 (s, 1H), 8.21 (br s, 1H)	513

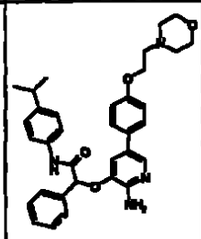
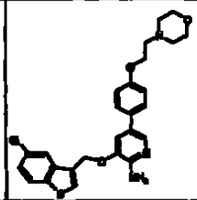
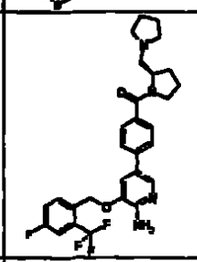
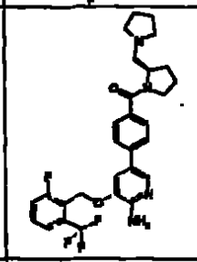
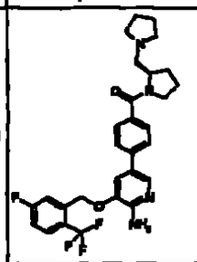
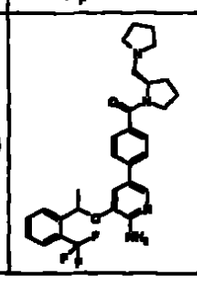
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-72		*N*-(1-[5-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-1*H*-indol-3-ylmethyl]-(3*S*)-pyrrolidin-3-yl)-acetamide	0.85	see examples	(300 MHz, $CDCl_3$) δ 1.71 (m, 1H), 1.91(s, 3H), 2.31 (m, 2H), 2.48 (m, 1H), 2.79(m, 2H), 3.11 (m, 1H), 3.66 (m, 2H), 4.66 (s, 2H), 5.31 (s, 2H), 7.06 (m, 1H), 7.20 (m, 2H), 7.45 (m, 4H), 7.66 (s, 1H), 7.99(s, 1H), 8.38 (s, 1H)	526
I-73		3-(2-Chloro-3,6-difluoro-benzyloxy)-5-(3-piperidin-1-ylmethyl-1*H*-indol-5-yl)-pyridin-2-ylamine	0.74	see examples	(300 MHz, $CDCl_3$) δ 1.54 (m, 2H), 1.84 (m, 4H), 2.56(m, 4H), 3.60 (s, 2H), 4.68 (s, 2H), 5.30(s, 2H), 7.05 (m, 1H), 7.20 (m, 2H), 7.45 (m, 3H), 7.66(s, 1H), 7.89 (s, 1H), 8.49 (br s, 1H)	483
I-74		3-(2-Chloro-3,6-difluoro-benzyloxy)-5-(3-morpholin-4-ylmethyl-1*H*-indol-5-yl)-pyridin-2-ylamine	1.4	see examples	(300 MHz, $CDCl_3$) δ 2.72 (m, 4H), 3.80 (m, 6H), 4.70 (s, 2H), 5.33 (d, 2H), 7.07 (m, 1H), 7.20 (m, 1H), 7.35-7.55 (m, 4H), 7.86 (s, 1H), 8.00 (d, 1H), 8.23 (s, 1H)	485
I-75		3-(2-Chloro-3,6-difluoro-benzyloxy)-5-(3-pyrrolidin-1-ylmethyl-1*H*-indol-5-yl)-pyridin-2-ylamine	0.7	see examples	(300 MHz, $CDCl_3$) δ 1.86 (m, 4H), 2.79 (m, 4H), 4.01 (s, 2H), 4.83 (s, 2H), 5.30 (d, 2H), 7.05 (m, 1H), 7.16 (m, 1H), 7.30-7.60 (m, 4H), 7.80 (s, 1H), 8.00 (d, 1H), 8.54 (s, 1H)	469
I-76		5-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carboxylic acid ethyl ester	>20	see examples	(400 MHz, DMSO-d_6) δ 1.34 (t, 3H), 4.34 (m, 2H), 5.34 (s, 2H), 5.68 (s, 2H), 7.16 (s, 1H), 7.62 (m, 6H), 7.84 (d, 2H), 11.84 (s, 1H)	459
I-77		5-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carboxylic acid	1.62	see examples	(400 MHz, DMSO-d_6) δ 5.48 (s, 2H), 5.68 (s, 2H), 6.66 (s, 1H), 7.33 (d, 1H), 7.44 (m, 2H), 7.54 (m, 3H), 7.72 (s, 1H), 7.86 (s, 1H), 11.12 (s, 1H)	429
I-78		(5-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-2-yl)-(4-methyl-piperazin-1-yl)-methanone	0.18	see examples	(400 MHz, DMSO-d_6) δ 2.21 (s, 3H), 2.36 (m, 4H), 3.74 (m, 4H), 5.35 (s, 2H), 5.53 (s, 2H), 6.78 (s, 1H), 7.50 (m, 6H), 7.81 (s, 1H), 7.88 (s, 1H), 11.56 (s, 1H)	510
I-79		(5-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-2-yl)-[(3*R*)-3-dimethylamino-pyrrolidin-1-yl]-methanone	0.18	see examples	(400 MHz, DMSO-d_6) δ 1.60 (m, 1H), 2.12 (m, 1H), 2.21 (s, 6H), 2.74 (m, 1H), 3.25 (m, 1H), 3.53 (m, 1H), 3.78 (m, 1H), 4.02 (m, 1H), 5.36 (s, 2H), 5.54 (s, 2H), 6.96 (s, 1H), 7.46 (m, 3H), 7.56 (m, 3H), 7.86 (m, 2H),11.53 (s, 1H)	524

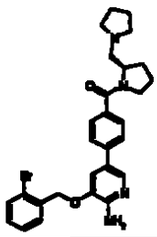
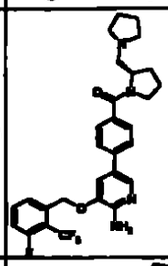
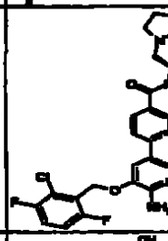
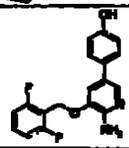
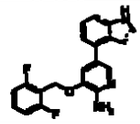
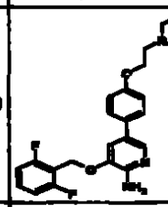
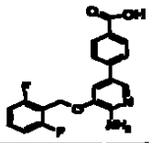
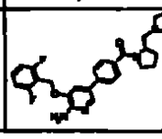
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-80		(5-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-2-yl)-[(2*R*)-3-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.079	see examples	(400 MHz, DMSO-d_6) δ 1.80 (m, 1H), 2.12 (m, 1H), 2.21 (s, 6H), 2.74 (m, 1H), 3.25 (m, 1H), 3.53 (m, 1H), 3.79 (m, 1H), 4.02 (m, 1H), 5.38 (s, 2H), 5.54 (s, 2H), 6.88 (s, 1H), 7.46 (m, 3H), 7.66 (m, 3H), 7.86 (m, 2H),11.53 (s, 1H)	624
I-81		5-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carboxylic acid (2-pyrrolidin-1-yl-ethyl)-amide	1.2	see examples	(400 MHz, DMSO-d_6) δ 1.66 (m, 4H), 2.61 (m, 4H), 2.66 (t, 2H), 3.39 (m, 2H), 7.11 (s, 1H), 7.45 (m, 2H), 7.65 (m, 3H), 7.80 (m, 1H), 7.82 (s, 1H), 7.86 (s, 1H), 8.46 (t, 1H), 11.66 (s, 1H)	624
I-82		5-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carboxylic acid (2-morpholin-4-yl-ethyl)-amide	1.8	see examples	(400 MHz, DMSO-d_6) δ 2.41 (m, 6H), 3.39 (m, 2H), 3.58 (m, 4H), 7.11 (s, 1H), 7.45 (m, 2H), 7.55 (m, 4H), 7.82 (s, 1H), 7.86 (s, 1H), 8.42 (t, 1H), 11.62 (s, 1H)	640
I-83		(1-(5-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carbonyl)-(3*S*)-pyrrolidin-3-yl)-carbonic acid tert-butyl ester	6	see examples	(400 MHz, DMSO-d_6) δ 1.38 (s, 9H), 1.84 (m, 1H), 1.99 (m, 2H), 3.18 (m, 2H), 3.76 (m, 2H), 5.37 (s, 2H), 5.52 (s, 2H), 6.82 (m, 1H), 7.26 (m, 1H), 7.48 (m, 2H), 7.56 (m, 3H), 7.81 (m, 1H), 7.86 (m, 2H), 11.62 (s, 1H)	696
I-84		(5-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-2-yl)-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone	0.14	see examples	(400 MHz, DMSO-d_6) δ 2.20 (m, 2H), 2.68 (m, 1H), 3.84 (m, 4H), 5.58 (s, 2H), 7.52 (m, 6H), 7.94 (m, 5H), 8.62 (m, 2H)	496
I-85		5-[6-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carboxylic acid (2-hydroxy-3-pyrrolidin-1-yl-propyl)-amide	0.7	see examples	(400 MHz, DMSO-d_6) δ 1.67 (m, 4H), 2.57 (m, 1H), 2.62 (m, 1H), 3.31 (m, 1H), 3.62 (m, 4H), 3.46 (m, 1H), 3.76 (m, 1H), 5.38 (s, 2H), 5.52 (s, 2H), 7.14 (s, 1H), 7.46 (m, 2H), 7.66 (m, 4H), 7.86 (m, 2H), 8.46 (t, 1H), 11.66 (s, 1H)	554
I-86		4-(6-Amino-5-benzyloxy-pyridin-3-yl)-phenol	8.7	see examples	(400 MHz, DMSO-d_6) δ 9.4 (s, 1H), 7.74 (d, *J* = 2 Hz, 1H), 7.52 (d, *J* = 7.2 Hz, 2H), 7.38 (m, 4H), 7.32 (m, 2H), 6.8 (d, *J* = 7.2 Hz, 2H), 5.66 (s, 2H), 5.22 (s, 2H)	293
I-87		3-Benzyloxy-5-phenyl-pyridin-2-ylamine		see examples	(400 MHz, DMSO-d_6) 7.84 (d, 1H), 7.66 (d, 2H), 7.51 (d, 2H), 7.38 (m, 5H), 7.31 (t, 1H), 7.25 (t, 1H), 5.83 (br s, 2H), 5.24 (s, 2H)	277
I-88		3-(3-Methoxy-benzyloxy)-5-phenyl-pyridin-2-ylamine		see examples	(400 MHz, DMSO-d_6) 7.86 (d, 1H), 7.66 (m, 2H), 7.38 (m, 3H), 7.26 (m, 2H), 7.06 (m, 2H), 6.86 (m, 1H), 5.84 (br s, 2H), 5.21 (s, 2H), 3.75 (s, 3H)	307

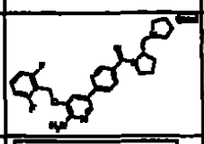
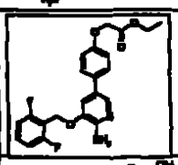
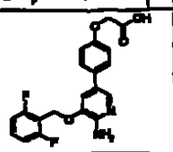
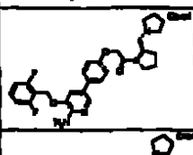
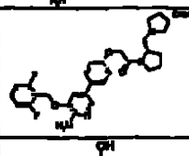
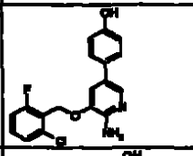
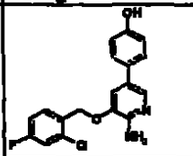
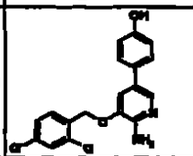
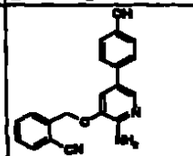
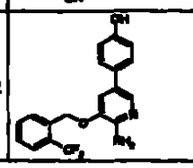
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-89		3-(2-Chloro-4-fluoro-benzyloxy)-5-phenyl-pyridin-2-ylamine	17	see examples	(400MHz, DMSO-d_6) δ 7.88 (s, 1H), 7.79 (m, 1H), 7.59 (m, 2H), 7.51 (dd, 1H), 7.40 (m, 3H), 7.27 (m, 2H), 5.84 (s, 2H), 5.24 (s,2H)	329
I-90		3-(2-Chloro-benzyloxy)-5-phenyl-pyridin-2-ylamine	48% at 20 uM	see examples	(400MHz, DMSO-d_6) δ 7.88 (d, 1H), 7.73 (m, 1H), 7.68 (m, 2H), 7.60 (m, 1H), 7.38 (m, 6H), 7.28 (m, 1H), 5.57 (s, 2H), 5.30 (s,2H)	311
I-91		3-(2,5-Dichloro-benzyloxy)-5-phenyl-pyridin-2-ylamine	48% at 20 uM	see examples	(400MHz, DMSO-d_6) δ 7.89 (d, 1H), 7.85 (d, 1H), 7.59 (m, 2H), 7.53 (d, 1H), 7.48 (d, 1H), 7.39 (m, 3H), 7.28 (m, 1H), 5.86 (s, 2H), 5.30 (s,2H)	345
I-92		3-(2-Chloro-5-trifluoromethyl-benzyloxy)-5-phenyl-pyridin-2-ylamine	>20	see examples	(400MHz, DMSO-d_6) δ 8.15 (s, 1H), 7.89 (d, 1H), 7.78 (d, 2H), 7.59 (m, 2H), 7.48 (d, 1H), 7.39 (m, 2H), 7.28 (m, 1H), 5.90 (s, 2H), 5.36 (s,2H)	379
I-93		3-(2,4-Dichloro-5-fluoro-benzyloxy)-5-phenyl-pyridin-2-ylamine	>20	see examples	(400MHz, DMSO-d_6) δ 7.86 (d, 1H), 7.68 (m, 2H), 7.60 (m, 2H), 7.44 (d, 1H), 7.39 (m, 2H), 7.26 (m, 1H), 6.01 (s, 2H), 5.24 (s,2H)	364
I-94		3-(2-Chloro-3-trifluoromethyl-benzyloxy)-5-phenyl-pyridin-2-ylamine	>20	see examples	(400MHz, DMSO-d_6) δ 8.10 (d, 1H), 7.69 (d, 1H), 7.65 (m, 1H), 7.60 (m, 3H), 7.45 (d, 1H), 7.39 (m, 2H), 7.28 (m, 1H), 5.93 (s, 2H), 5.37 (s,2H)	379
I-95		3-(2-Chloro-3,6-difluoro-benzyloxy)-5-phenyl-pyridin-2-ylamine	0.64	see examples	(400MHz, DMSO-d_6) δ 7.89 (d, 1H), 7.57 (m, 4H), 7.40 (m, 3H), 7.28 (m, 1H), 5.72 (s, 2H), 5.29 (s,2H)	347
I-96		3-(3,4-Dichloro-benzyloxy)-5-phenyl-pyridin-2-ylamine	16.2	see examples	(400MHz, DMSO-d_6) δ 7.88 (d, 1H), 7.84 (d, 1H), 7.65 (m, 1H), 7.57 (m, 3H), 7.39 (m, 3H), 7.28 (m, 1H), 5.98 (s, 2H), 5.24 (s,2H); MS m/z 345(M+1).	345
I-97		2-(2-Amino-5-phenyl-pyridin-3-yloxymethyl)-benzonitrile	12.2	see examples	(400MHz, DMSO-d_6) δ 7.90 (dd, 2H), 7.82 (d, 1H), 7.75 (m, 1H), 7.56 (m, 3H), 7.48 (d, 1H), 7.40 (m, 2H), 7.28 (m, 1H), 6.65 (s, 2H), 5.38 (s,2H)	302
I-98		3-(2-Chloro-6-fluoro-3-methyl-benzyloxy)-5-phenyl-pyridin-3-ylamine	7.6	see examples	(400MHz, DMSO-d_6) δ 7.89 (d, 1H), 7.61 (m, 2H), 7.53 (d, 1H), 7.43 (m, 3H), 7.25 (m, 2H), 6.66 (s, 2H), 5.27 (s,2H), 2.34 (s, 3H)	342
I-99		5-Phenyl-3-(2,3,6-trifluoro-benzyloxy)-pyridin-2-ylamine	3.9	see examples	(400MHz, DMSO-d_6) δ 7.88 (d, 1H), 7.61 (m, 3H), 7.52 (d, 1H), 7.40 (m, 2H), 7.25 (m, 2H), 5.75 (s, 2H), 5.28 (s,2H)	331

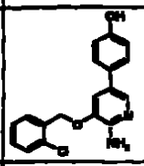
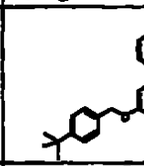
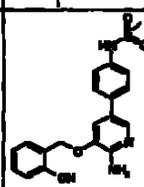
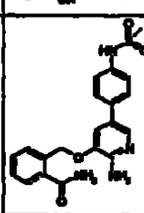
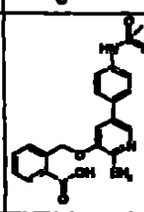
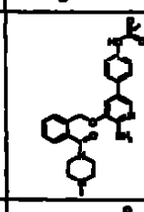
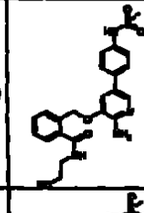
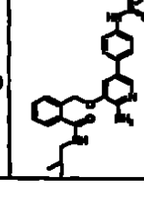
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-100		3-(2,6-Difluoro-benzyloxy)-5-phenyl-pyridin-2-ylamine	6.3	see examples	(400MHz, DMSO-d_6) δ 7.88 (d, 1H), 7.61 (m, 2H), 7.51 (m, 2H), 7.40 (m, 2H), 7.26 (m, 1H), 7.16 (m, 2H), 6.98 (s, 2H), 5.23 (s,2H)	314
I-101		3-(2,6-Difluoro-3-methyl-benzyloxy)-5-phenyl-pyridin-2-ylamine	12	see examples	(400MHz, DMSO-d_6) δ 7.88 (d, 1H), 7.80 (m, 2H), 7.51 (d, 1H), 7.40 (m, 3H), 7.27 (m,1H), 7.07 (m, 1H), 6.98 (s, 2H), 5.21 (s,2H)	328
I-102		3-(3-Chloro-2,6-difluoro-benzyloxy)-5-phenyl-pyridin-2-ylamine	6.6	see examples	(400MHz, DMSO-d_6) δ 7.88 (d, 1H), 7.74 (m, 1H), 7.61 (m,2H), 7.51 (d, 1H), 7.40 (m, 2H), 7.27 (m,2H), 6.78 (s, 2H), 5.28 (s, 2H)	347
I-103		3-(2-Chloro-6-fluoro-benzyloxy)-5-phenyl-pyridin-2-ylamine	7.91	see examples	(400MHz, DMSO-d_6) δ 7.88 (d, 1H), 7.81 (m, 2H), 7.62 (d, 1H), 7.49 (m,1H), 7.40 (m, 3H), 7.30 (m, 2H), 5.87 (s, 2H), 5.27 (s, 2H)	329
I-104		3-(3-Fluoro-4-methoxy-benzyloxy)-5-phenyl-pyridin-2-ylamine	15	see examples	(400 MHz, DMSO-d_6) δ 7.84 (d, 1H), 7.66 (m, 1H), 7.43 (d, 1H), 7.38 (m,3H), 7.26 (m, 2H), 7.10 (m, 2H), 5.82 (s, 2H), 5.15 (s, 2H)	325
I-105		*N*-[3-(2-Amino-5-phenyl-pyridin-3-yloxymethyl)-phenyl]-methanesulfonamide	>20	see examples	(400 MHz, DMSO-d_6) δ 9.76 (s, 1H), 7.85 (d, *J* = 1.8 Hz, 1H), 7.57 (d, 2H), 7.35 (m, 5H), 7.28 (m, 2H), 7.15 (d, 1H), 6.85 (br s, 2H), 5.22 (s, 2H), 2.99 (s, 3H)	370
I-106		5-[4-(2-Morpholin-4-yl-ethoxy)-phenyl]-3-(3-nitro-benzyloxy)-pyridin-2-ylamine	12.6	see examples	(DMSO-d_6) δ 2.50 (m, 4H), 2.62 (m, 2H), 3.57 (t, 4H), 4.09 (t, 2H), 5.37 (s, 2H), 5.55 (s, 2H),6.96 (d, 2H), 7.38 (d, 1H), 7.48 (d, 2H), 7.69 (t, 1H), 7.81 (d, 1H), 8.01 (m, 1H), 8.17 (m, 1H), 8.26 (m, 1H)	451
I-107		5-[4-(2-Morpholin-4-yl-ethoxy)-phenyl]-3-(naphthalen-1-ylmethoxy)-pyridin-2-ylamine	7.7	see examples	(DMSO-d_6) δ 2.50 (m, 4H), 2.69 (t, 2H), 3.57 (t, 4H), 4.10 (t, 2H), 5.06 (s, 2H), 5.57 (s, 2H), 6.97 (d, 2H), 7.48-7.61 (m, 5H), 7.76-7.82 (m, 2H), 7.89-7.96 (m, 2H), 8.20 (dd, 1H)	456
I-108		3-(2-Chloro-3,6-difluoro-benzyloxy)-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine	0.21	see examples	(400 MHz, $CDCl_3$) δ 2.60 (m, 4H), 2.83 (t, 2H), 3.74 (t, 4H), 4.19 (t, 2H), 4.83 (s, 2H), 5.27 (d, 2H), 6.98 (d, 2H), 7.02-7.10 (m, 1H), 7.19-7.22 (m, 1H), 7.30 (2, 2H), 7.44 (d, 2H), 7.91 (d, 1H)	476

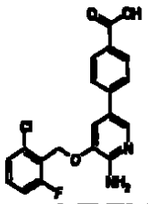
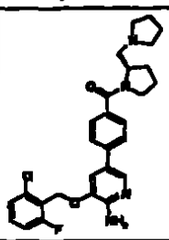
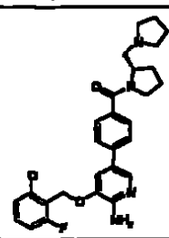
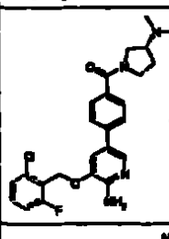
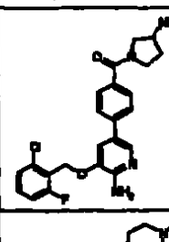
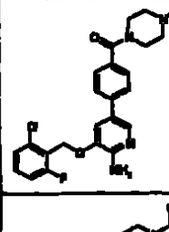
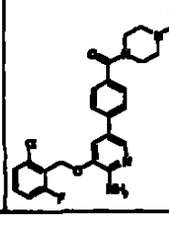
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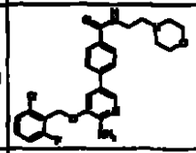
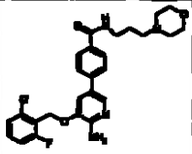
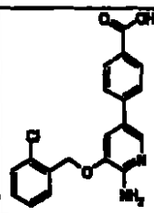
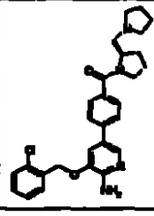
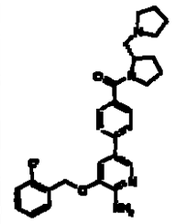
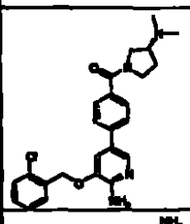
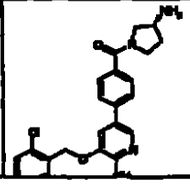
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-109		2-[2-Amino-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-3-yloxy]-*N*-(4-isopropyl-phenyl)-2-phenyl-acetamide	>20	see examples	(400 MHz, DMSO-d_6) δ 1.15 (d, 6H), 2.50 (m, 4H), 2.68 (m, 2H), 2.77-2.89 (m, 1H), 3.57 (t, 6H), 4.08 (t, 2H), 6.15 (s, 1H), 6.20 (s, 2H), 6.93 (d, 2H), 7.17 (d, 1H), 7.30-7.44 (m, 3H), 7.48(d, 2H), 7.58 (d, 2H), 7.79 (d, 1H)	568
I-110		3-(5-Chloro-benzo[*b*]thiophen-3-ylmethoxy)-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine	2.4	see examples	(400 MHz, DMSO-d_6) δ 2.50 (m, 4H), 2.70 (m, 2H), 3.58 (t, 4H), 4.11 (t, 2H), 5.46 (s, 2H), 5.82 (s, 2H), 6.68 (d, 2H), 7.43 (dd, 1H), 7.50-7.56 (m, 3H), 7.80(d, 1H), 8.05 (d, 1H), 8.11 (d, 1H), 8.16 (s, 1H)	496.5
I-111		{4-[6-Amino-5-(4-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	1.51	see examples	(400 MHz, DMSO-d_6) δ 7.94 (s, 2H), 7.71 (m, 4H), 7.44 (m, 3H), 5.92 (s, 2H), 5.38 (s, 2H), 4.21 (m, 1H), 3.52 (m, 2H), 2.89 (m, 5H), 1.98 (m, 2H), 1.84 (m, 3H), 1.68 (m, 4H)	543
I-112		{4-[6-Amino-5-(2-fluoro-6-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.15	see examples	(400 MHz, DMSO-d_6) δ 7.94 (s, 1H), 7.69 (m, 3H), 7.58 (s, 1H), 7.50 (m, 2H), 5.72 (s, 2H), 5.28 (s, 2H), 4.16 (m, 1H), 3.47 (m, 2H), 2.63 (m, 5H), 1.98 (m, 2H), 1.88 (m, 3H), 1.68 (m, 4H)	543
I-113		{4-[6-Amino-5-(5-fluoro-3-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	1.27	see examples	(400 MHz, DMSO-d_6) δ 7.95 (s, 1H), 7.85 (m, 2H), 7.63 (m, 2H), 7.48 (m, 2H), 7.42 (m, 2H), 6.04 (s, 2H), 5.36 (s, 2H), 4.16 (m, 1H), 3.44 (m, 2H), 2.62 (m, 5H), 1.98 (m, 2H), 1.88 (m, 3H), 1.66 (m, 4H)	543
I-114		{4-[6-Amino-5-[1-(2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.33	see examples	(400 MHz, DMSO-d_6) δ 7.85 (d, 1H), 7.81 (s, 1H), 7.76 (m, 2H), 7.41 (m, 5H), 7.03 (s, 1H), 6.16 (s, 2H), 5.81 (m, 1H), 4.10 (m, 1H), 3.41 (m, 2H), 2.89 (m, 5H), 1.94 (m, 2H), 1.82 (m, 3H), 1.64 (d, 3H), 1.48 (m, 4H)	639

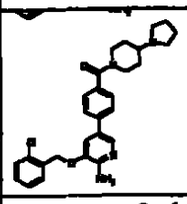
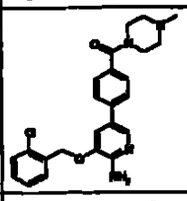
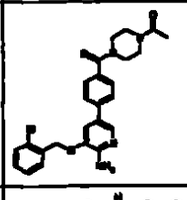
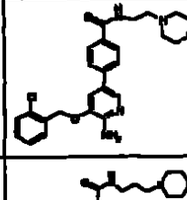
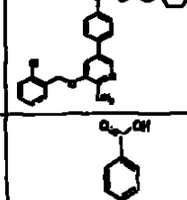
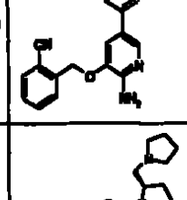
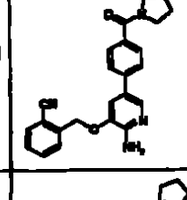
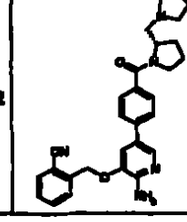
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS *m/z* (M+1)
I-115		(4-[6-Amino-5-(2-bromo-benzyloxy)-pyridin-3-yl]-phenyl)-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	1.76	see examples	(400 MHz, DMSO-d_6) δ 7.74 (s, 1H), 7.58 (m, 3H), 7.45 (m, 6H), 7.31 (m, 1H), 5.82 (s, 2H), 5.25 (s, 2H), 4.16 (m, 1H), 3.43 (m, 2H), 2.82 (m, 5H), 1.94 (m, 2H), 1.82 (m, 3H), 1.65 (m, 4H)	537
I-116		(4-[6-Amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl)-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.025	see examples	(400 MHz, DMSO-d_6) δ 7.92 (s, 1H), 7.66 (m, 4H), 7.46 (m, 4H), 6.89 (s, 2H), 5.39 (s, 2H), 4.19 (m, 1H), 3.60 (m, 2H), 2.84 (m, 5H), 1.95 (m, 2H), 1.83 (m, 3H), 1.64 (m, 4H)	643
I-117		(4-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.063	see examples	(400MHz, DMSO-d_6) δ 7.95 (d, 1H), 7.69 (d, 2H), 7.58 (m, 2H), 7.50 (d, 2H), 7.40 (m, 1H), 5.61 (s, 2H), 5.29 (s, 2H), 4.36 (m, 1H), 3.5 (d, 2H), 2.67 (d, 2H), 2.71 (d, 2H), 1.7-2.0 (m, 10H)	627
I-118		4-[6-Amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenol	3.79	see examples	(400 MHz, DMSO-d_6) δ 9.38 (s, 1H), 7.77 (d, *J* = 2 Hz 1H), 7.52 (m, 2H), 7.40 (m, 3H), 7.17 (m, 2H), 6.79 (m, 2H), 5.53 (br. s, 2H), 5.20 (s, 2H)	329
I-119		3-(2,6-Difluoro-benzyloxy)-5-(1H-indol-4-yl)-pyridin-2-ylamine	5.8	see examples	(400 MHz, DMSO-d_6) δ 7.91 (d, *J* = 2 Hz, 1H), 7.81 (m, 3H), 7.45 (d, *J* = 2 Hz, 1H), 7.17 (m, 2H), 6.38 (m, 2H), 5.55 (s, 2H), 5.21 (s, 2H), 4.10 (t, 2H), 3.57 (t, 4H), 2.69 (t, 2H), 2.48 (t, 4H)	442
I-120		3-(2,6-Difluoro-benzyloxy)-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine		see examples	(400 MHz, DMSO-d_6) δ 11.16 (s, 1H), 7.98 (d, *J* = 2 Hz, 1H), 7.62 (m, 1H), 7.44 (d, *J* = 2 Hz, 1H), 7.36 (dd, 1H), 7.34 (m, 1H), 7.18 (m, 2H), 7.13 (dd, 1H), 7.02 (dd, 1H), 6.49 (m, 1H), 5.68 (s, 2H), 5.22 (s, 2H)	362
I-121		4-[6-Amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid		see examples	(400 MHz, DMSO-d_6) δ 12.85 (s, 1H), 7.94 (d, *J* = 2Hz, 1H), 7.89 (dd, 2H), 7.71 (dd, 2H), 7.55 (d, *J* = 2Hz, 1H), 7.47 (m, 1H), 7.13 (m, 2H), 5.83 (s, 2H), 5.19 (s, 2H)	357
I-122		(4-[6-Amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	1.21	see examples	(400 MHz, DMSO-d_6) δ 7.94 (d, 1H), 7.68 (dd, 2H), 7.56 (m, 1H), 7.51 (m, 3H), 7.18 (m, 2H), 5.79 (s, 2H), 5.29 (s, 2H), 3.48 (m, 1H), 2.86 (m, 4H), 2.48 (d, 2H), 1.88 (m, 10H)	493

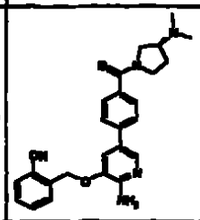
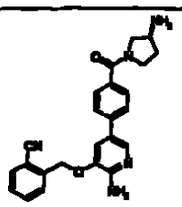
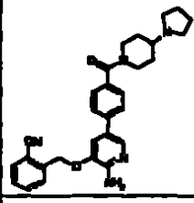
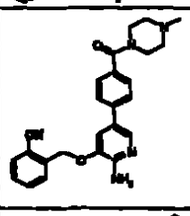
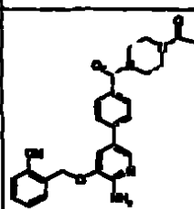
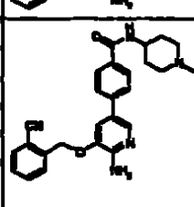
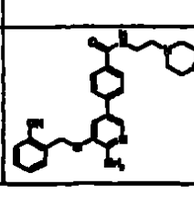
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-123		(4-[6-Amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-[(2S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	1.36	see examples	(400 MHz, DMSO-d_6) δ 7.94 (d, 1H), 7.88 (dd, 2H), 7.58 (m, 1H), 7.51 (m, 3H), 7.16 (m, 2H), 5.78 (s, 2H), 5.24 (s, 2H), 4.8 (m, 1H), 3.5 (m, 2H), 2.52 (d, 4H), 1.86 (m, 10H)	493
I-124		(4-[6-Amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenoxy)-acetic acid ethyl ester		see examples	(400 MHz, DMSO-d_6) δ 7.81 (d, J = 2 Hz, 1H), 7.52 (m, 3H), 7.16 (m, 1H), 6.86 (m, 2H), 5.70 (br. s, 2H), 5.23 (s, 2H), 4.79 (s, 2H), 2.68 (q, 4H), 1.21 (t, 3H)	415
I-125		(4-[6-Amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenoxy)-acetic acid	14.7	see examples	(400 MHz, DMSO-d_6) δ 7.79 (d, 1H), 7.51 (m, 1H), 7.47 (m, 1H), 7.44 (m, 2H), 7.17 (m, 2H), 7.05 (m, 2H), 5.96 (br. s, 2H), 5.21 (s, 2H), 4.25 (s, 2H)	387
I-126		2-(4-[6-Amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenoxy)-1-[(2R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-ethanone	3.56	see examples	(400 MHz, DMSO-d_6) δ 7.81 (d, 1H), 7.51 (m, 3H), 7.45 (d, 1H), 7.16 (m, 2H), 6.90 (m, 2H), 5.85 (s, 2H), 5.22 (s, 2H), 4.80 (dd, 2H), 4.29 (m, 1H), 3.53 (m, 2H), 3.20 (m, 4H), 1.93 (m, 10H)	523
I-127		2-(4-[6-Amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenoxy)-1-[(2S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-ethanone	5.43	see examples	(400 MHz, DMSO-d_6) δ 7.81 (d, 1H), 7.52 (m, 3H), 7.46 (d, 1H), 7.18 (m, 2H), 7.00 (m, 2H), 5.88 (s, 2H), 5.22 (s, 2H), 4.80 (dd, 2H), 4.60 (m, 1H), 3.53 (m, 2H), 2.19 (m, 4H), 1.96 (m, 10H)	523
I-128		4-[6-Amino-5-(3-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-phenol	3.98	see examples	(400MHz, DMSO-d_6) δ 9.38 (s, 1H), 7.77 (d, 1H), 7.60 (m, 1H), 7.42 (m, 4H), 7.39 (m, 1H), 6.80 (m, 2H), 5.80 (s, 2H), 5.24 (s, 2H)	345
I-129		4-[6-Amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-phenol	19	see examples	(DMSO-d_6) δ 5.21 (s, 2H), 5.67 (s, 2H), 6.86 (d, 2H), 7.26 (t, 1H), 7.34 (s, 1H), 7.41 (d, 2H), 7.50 (d, 1H), 7.78 (m, 2H), 9.38 (s, 1H)	345
I-130		4-[6-Amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenol	9/>20	see examples	(DMSO-d_6) δ 5.21 (s, 2H), 5.71 (s, 2H), 6.81 (d, 2H), 7.40 (m, 6H), 7.74 (m, 2H), 9.38 (s, 1H)	361
I-131		2-[2-Amino-5-(4-hydroxy-phenyl)-pyridin-3-yloxymethyl]-benzonitrile	18	see examples	(DMSO-d_6) δ 5.35 (s, 2H), 5.68 (s, 2H), 6.77 (d, 2H), 7.41 (m, 3H), 7.54 (t, 1H), 7.76 (m, 3H), 7.92 (d, 1H), 9.38 (s, 1H)	318
I-132		4-[6-Amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenol	3.67	see examples	(400 MHz, DMSO-d_6) δ 5.32 (s, 2H), 5.69 (s, 2H), 6.78 (d, 2H), 7.28 (s, 1H), 7.36 (d, 2H), 7.57 (t, 1H), 7.72 (t, 1H), 7.78 (m, 2H), 7.86 (m, 1H), 9.36 (s, 1H)	361

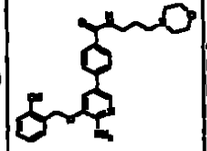
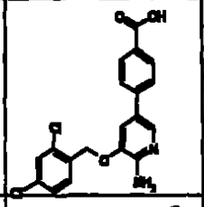
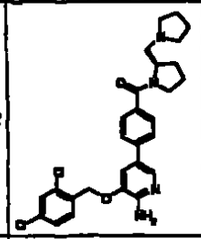
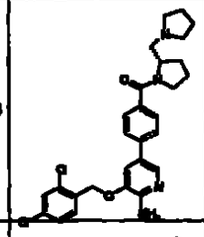
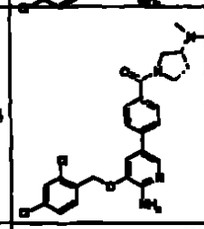
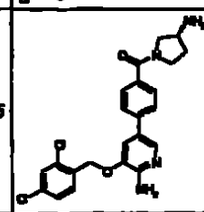
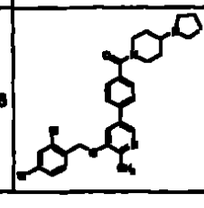
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-133		4-[6-Amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenol	13.8	see examples	(DMSO-d_6) δ 5.25 (s, 2H), 5.69 (s, 2H), 6.78 (d, 2H), 7.38 (m, 6H), 7.50 (m, 1H), 7.71 (m, 1H), 7.76 (s, 1H), 9.38 (s, 1H)	328
I-134		4-[6-Amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-phenol	4	see examples	(DMSO-d_6) δ 1.28 (s, 9H), 5.16 (s, 2H), 5.63 (s, 2H), 6.78 (d, 2H), 7.40 (m, 7H), 7.72 (s, 1H), 9.36 (s, 1H)	349
I-135		*N*-(4-[6-Amino-5-(2-cyano-benzyloxy)-pyridin-3-yl]-phenyl)-methanesulfonamide	4.16	see examples	(DMSO-d_6) δ 2.99 (s, 3H), 5.36 (s, 2H), 5.82 (s, 2H), 7.24 (d, 2H), 7.42 (s, 1H), 7.58 (m, 3H), 7.75 (t, 1H), 7.99 (m, 3H), 9.70 (s, 1H)	393
I-136		2-[2-Amino-5-(4-methanesulfonylamino-phenyl)-pyridin-3-yloxymethyl]-benzamide	>20	see examples	(DMSO-d_6) δ 2.98 (s, 3H), 5.37 (s, 2H), 5.75 (s, 2H), 7.15 (d, 2H), 7.30 (c, 1H), 7.48 (m, 6H), 7.20 (d, 1H), 7.80 (c, 1H), 7.90 (s, 1H)	413
I-137		2-[2-Amino-5-(4-methanesulfonylamino-phenyl)-pyridin-3-yloxymethyl]-benzoic acid	>20	see examples	(DMSO-d_6) δ 3.00 (s, 3H), 5.85 (s, 2H),7.26 (d, 2H), 7.47 (m, 3H), 7.60 (m, 4H), 7.72 (m, 1H), 7.82 (s, 1H), 7.94 (d, 1H), 9.84 (s, 1H)	414
I-138		*N*-(4-[6-Amino-5-[2-(4-methyl-piperazine-1-carbonyl)-benzyloxy]-pyridin-3-yl]-phenyl)-methanesulfonamide	>20	see examples	(DMSO-d_6) δ 2.06 (s, 3H), 2.35 (m, 2H), 2.66 (s, 3H), 3.15 (m, 2H), 3.38 (m, 2H), 3.69 (m, 2H), 5.17 (br s, 2H), 5.78 (s, 2H), 7.23 (d, 2H), 7.28 (m, 1H), 7.38 (s, 1H), 7.43 (m, 2H), 7.57 (m, 4H), 7.84 (s, 1H)	496
I-139		2-[2-Amino-5-(4-methanesulfonylamino-phenyl)-pyridin-3-yloxymethyl]-*N*-(2-hydroxy-ethyl)-benzamide	>20	see examples	(DMSO-d_6) δ 2.99 (s, 3H), 3.28 (m, 2H), 3.48 (m, 2H), 4.70 (s, 1H), 5.30 (s, 2H), 5.78 (s, 2H), 7.23 (d, 2H), 7.32 (s, 1H), 7.39 (m, 1H), 7.47 (m, 2H), 7.53 (m, 2H), 7.62 (d, 1H), 7.83 (s, 1H), 8.37 (t, 1H), 9.72 (br s, 1H)	457
I-140		2-[2-Amino-5-(4-methanesulfonylamino-phenyl)-pyridin-3-yloxymethyl]-*N*-isobutyl-benzamide	>20	see examples	(DMSO-d_6) δ 0.84 (d, 6H), 1.78 (m, 1H), 2.82 (s, 3H), 3.03 (t, 2H), 5.28 (s, 2H), 5.72 (s, 2H), 7.12 (d, 2H), 7.24 (s, 1H), 7.42 (m, 6H), 7.82 (d, 1H), 7.79 (s, 1H), 8.41 (t, 1H), 9.68 (s, 1H)	469

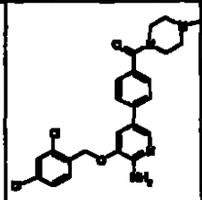
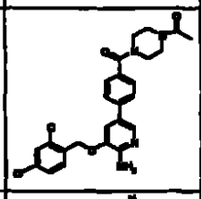
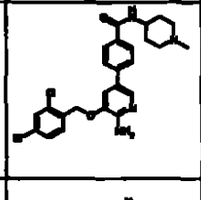
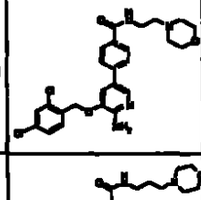
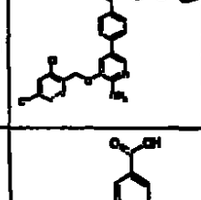
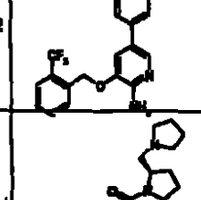
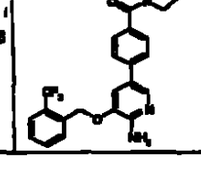
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-141		4-[5-Amino-6-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-benzoic acid		see examples	(400MHz, DMSO-d_6) δ 5.25 (s, 2H, CH_2), 6.82 (br s, 2H, NH_2), 6.30 - 8.00 (multiplets, 6H, aromatic)	373
I-142		{4-[5-Amino-6-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.83	see examples	(300 MHz, $CDCl_3$) δ 7.96 (d, 1H), 7.57 (m, 4H), 7.10 (m, 3H), 7.04(t, 1H), 6.30 (s, 2H), 4.83 (s, 2H), 4.46 (m, 1H), 3.40 (m, 2H), 2.90 (m, 4H), 2.2 1.8 (m, 10H)	509
I-143		{4-[5-Amino-6-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	13	see examples	(300 MHz, $CDCl_3$) δ 7.96 (d, 1H), 7.57 (m, 4H), 7.10 (m, 3H), 7.04(t, 1H), 6.30 (s, 2H), 4.83 (s, 2H), 4.46 (m, 1H), 3.40 (m, 2H), 2.90 (m, 4H), 2.2 1.5 (m, 10H)	509
I-144		{4-[5-Amino-6-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone	1.7	see examples	(300 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.58 (m, 4H), 7.36 (m, 3H), 7.05(t, 1H), 6.30 (s, 2H), 5.07 (s, 2H), 3.9 (m, 1H), 3.6 (m, 2H), 3.4 (m, 1H), 3.0 (m, 1H), 2.37 (s, 3H), 2.27 (s, 3H), 1.8 (m, 2H)	470
I-145		{4-[5-Amino-6-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone	0.83	see examples		441
I-146		{4-[5-Amino-6-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone	1.94	see examples	(300 MHz, $CDCl_3$) δ 7.93 (d, *J* = 1.7 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 2H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.28 (m, 3H), 7.07 (t, *J* = 8.8 Hz), 6.30(s, 2H), 5.05 (br s, 2H), 3.75 (m, 4H), 2.48 (m, 4H), 2.34 (s, 3H)	455
I-147		1-(4-{4-[5-Amino-6-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-benzoyl}-piperazin-1-yl)-ethanone	1.46	see examples	(300 MHz, $CDCl_3$) δ 7.91 (d, *J* = 1.7 Hz, 1H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.50 (d, *J* = 8.2 Hz, 2H), 7.35 (m, 3H), 7.06 (t, *J* = 8.2 Hz), 5.42 (br s, 2H), 5.22 (s, 2H), 3.60 (m, 8H), 2.14 (s, 3H)	484

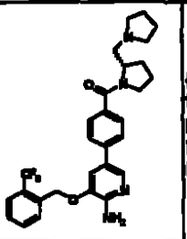
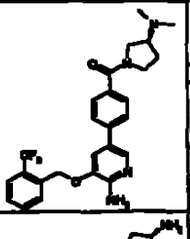
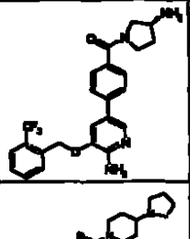
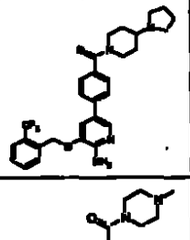
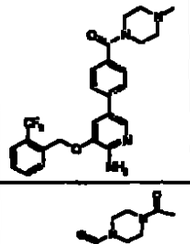
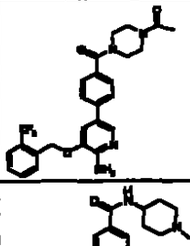
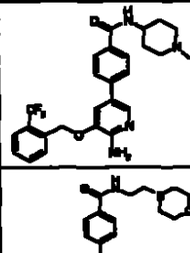
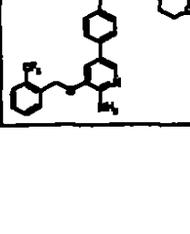
No.	Structure	Name	Mist IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-148		4-[6-Amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide	6.4	see examples	(300 MHz, $CDCl_3$) δ 7.96 (d, *J* = 1.7 Hz, 1H), 7.85 (d, *J* = 8.2 Hz, 2H), 7.65 (d, *J* = 8.2 Hz, 2H), 7.30 (m, 2H), 7.24 (d, J = 1.7 Hz, 1H), 7.06 (m, 1H), 6.95 (br t, 1H), 5.32 (s, 2H), 5.06 (br s, 2H), 3.82 (m, 4H), 3.64 (m, 2H), 2.76 (m, 2H), 2.65 (m, 4H)	485
I-149		4-[6-Amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide	5.8	see examples	(300 MHz, $CDCl_3$) δ 8.02 (br t, 1H), 7.95 (d, *J* = 1.7 Hz, 1H), 7.80 (d, *J* = 8.3 Hz, 2H), 7.68 (d, *J* = 8.3 Hz, 2H), 7.38 (d, J = 1.7 Hz, 1H), 7.30 (m, 2H), 7.08 (m,1H), 6.95 (br t, 1H), 5.32 (s, 2H), 5.10 (br s, 2H), 3.78 (m, 4H), 3.62 (m, 2H), 2.64 (m, 6H), 1.87 (m, 2H)	499
I-150		4-[6-Amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-benzoic acid		see examples	(400 MHz, DMSO-d_6) δ 5.30 (s, 2H, CH_2), 6.96 (br s, 2H, NH_2), 7.35 - 7.98 (multiplets, 10H, aromatic).	353 (M-1)
I-151		{4-[6-Amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.87	see examples	(300 MHz, $CDCl_3$) δ 7.98 (d, *J* = 1.8 Hz, 1H), 7.52 (m, 6H), 7.25 (m, 2H), 7.21(d, J = 1.8 Hz, 1H), 5.28 (s, 2H), 4.88 (br s, 2H), 4.32 (m, 1H), 3.62 (m, 2H), 2.89 (m, 4H), 2.2-1.8 (m, 10H).	491
I-152		{4-[6-Amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	2.3	see examples	(300 MHz, $CDCl_3$) δ 7.98 (d, *J* = 1.8 Hz, 1H), 7.82 (m, 6H), 7.25 (m, 2H), 7.21(d, J = 1.8 Hz, 1H), 5.28 (s, 2H), 4.88 (br s, 2H), 4.32 (m, 1H), 3.62 (m, 2H), 2.89 (m, 4H), 2.2-1.8 (m, 10H). MS m/z 491 (M+1).	491
I-153		{4-[6-Amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone	12.7	see examples	(300 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.83 (m, 6H), 7.33 (m, 2H), 7.27(s, 1H), 5.28 (s, 2H), 4.84 (br s, 2H), 3.90 (m, 1H), 3.80 (m, 2H), 3.45 (m, 1H), 2.85 (m, 1H), 2.32 (s, 3H), 2.23 (s, 3H), 1.89 (m, 2H)	451
I-154		{4-[6-Amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone	1.44	see examples		423

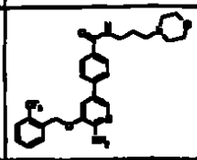
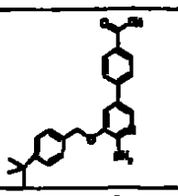
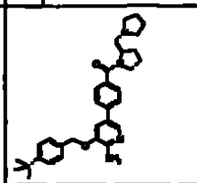
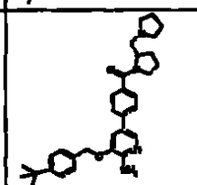
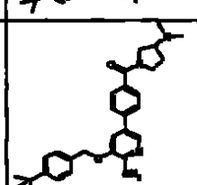
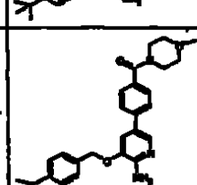
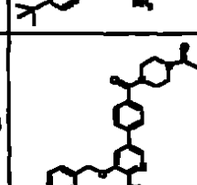
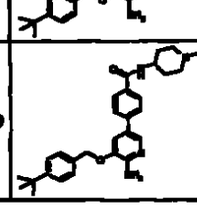
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-156		(4-[6-Amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	1.8	see examples	(300 MHz, $CDCl_3$) δ 7.98 (d, J = 1.8 Hz, 1H), 7.47 (m, 6H), 7.32 (m, 2H), 7.21(d, J = 1.8 Hz, 1H), 5.28 (s, 2H), 4.66 (br s, 2H), 3.95 (m, 4H), 2.55 (m, 4H), 2.30 (m, 1H), 1.95 (m, 2H), 1.76 (m, 4H), 1.52 (m, 2H).	491
I-158		(4-[6-Amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone	2.1	see examples	(300 MHz, $CDCl_3$) δ 7.94 (d, J = 1.8 Hz, 1H), 7.49 (m, 6H), 7.32 (m, 2H), 7.21(d, J = 1.8 Hz, 1H), 5.27 (s, 2H), 4.00 (br s, 2H), 3.80 (m, 4H), 2.60 (m, 4H), 2.35 (s, 3H)	437
I-157		1-(4-{4-[6-Amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-benzoyl}-piperazin-1-yl)-ethanone	3.8	see examples	(300 MHz, $CDCl_3$) δ 7.95 (d, J = 1.8 Hz, 1H), 7.51 (m, 6H), 7.33 (m, 2H), 7.21(d, J = 1.8 Hz, 1H), 5.27 (s, 2H), 4.64 (br s, 2H), 3.66 (m, 8H), 2.14 (s, 3H)	465
I-155		4-[6-Amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide	8.9	see examples	(300 MHz, $CDCl_3$) δ 7.98 (d, J = 1.8 Hz, 1H), 7.84 (d, J = 8.3 Hz, 2H), 7.55 (d, J = 8.3 Hz, 2H), 7.51 (m, 1H), 7.43 (m, 1H), 7.34 (m, 2H), 7.24(d, J = 1.8 Hz, 1H), 7.01 (br t, 1H), 5.27 (s, 2H), 5.16 (br s, 2H), 3.77 (m, 4H), 3.61 (m, 2H), 3.38 (m, 2H), 2.70 (m, 2H), 2.60 (m, 4H)	457
I-159		4-[6-Amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-N-(3-morpholin-4-yl-propyl)-benzamide	4.5	see examples	(300 MHz, $CDCl_3$) δ 7.95 (d, J = 1.8 Hz, 1H), 7.84 (d, J = 8.3 Hz, 2H), 7.55 (d, J = 8.3 Hz, 2H), 7.51 (m, 2H), 7.43 (m, 1H), 7.34 (m, 2H), 7.24(d, J = 1.8 Hz, 1H), 5.27 (s, 2H), 4.97 (br s, 2H), 3.75 (m, 4H), 3.59 (m, 2H), 3.25 (m, 2H), 2.57 (m, 4H), 1.83 (m, 2H).	481
I-160		4-[6-Amino-5-(2-cyano-benzyloxy)-pyridin-3-yl]-benzoic acid		see examples	(400 MHz, DMSO-d_6) δ 5.36 (s, 2H, CH_2), 5.95 (br s, 2H, NH_2), 7.50-8.00 (multiplets, 10H, aromatic)	346
I-161		2-[2-Amino-5-[4-((2R)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl]-benzonitrile	1.2	see examples	(300 MHz, $CDCl_3$) δ 7.99 (d, J = 1.8 Hz, 1H), 7.76 (d, J = 7.5 Hz, 2H), 7.50 (m, 6H), 7.24(d, J = 1.8 Hz, 1H), 5.35 (s, 2H), 4.89 (br s, 2H), 4.48 (m, 1H), 3.52 (m, 2H), 3.24 (m, 4H), 2.2-1.5 (m, 10H)	482
I-162		2-[2-Amino-5-[4-((2S)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl]-benzonitrile	2	see examples	^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (d, J = 1.8 Hz, 1H), 7.76 (d, J = 7.5 Hz, 2H), 7.50 (m, 6H), 7.24(d, J = 1.8 Hz, 1H), 5.35 (s, 2H), 4.89 (br s, 2H), 4.48 (m, 1H), 3.52 (m, 2H), 3.24 (m, 4H), 2.2-1.5 (m, 10H).	482

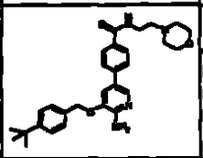
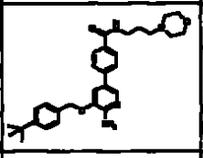
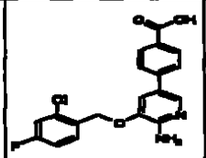
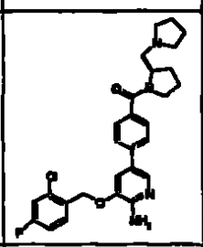
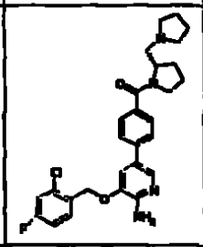
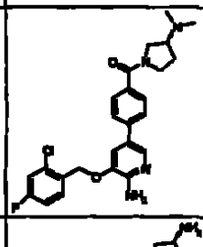
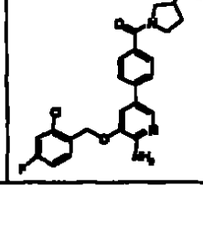
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-163		2-[2-Amino-5-[4-((3S)-3-dimethylamino-pyrrolidine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl]-benzonitrile	>20	see examples	(300 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.76 (d, J = 7.8 Hz, 2H), 7.50 (m, 6H), 7.26(s, 1H), 5.36 (s, 2H), 4.99 (br s, 2H), 3.90 (m, 1H), 3.60 (m, 2H), 3.48 (m, 1H), 2.85 (m, 1H), 2.32 (s, 3H), 2.23 (s, 3H), 1.99 (m, 2H)	442
I-164		2-[2-Amino-5-[4-((3S)-3-amino-pyrrolidine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl]-benzonitrile	2.05	see examples	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.4 Hz,, 1H), 7.76 (d, J = 7.5 Hz, 2H), 7.50 (m, 6H), 7.24(d, J = 1.4 Hz, 1H), 5.35 (s, 2H), 4.91 (br s, 2H), 3.70 (m, 4H), 2.16 (m, 1H), 2.23 (s, 2H), 1.25 (m, 1H), 1.06 (m, 1H)	414
I-165		2-[2-Amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl]-benzonitrile	3.9	see examples	(300 MHz, $CDCl_3$) δ 7.97 (d, J = 1.7 Hz,, 1H), 7.76 (d, J = 7.5 Hz, 2H), 7.66 (m, 2H), 7.51 (m, 2H), 7.46 (m, 2H), 7.22(d, J = 1.4 Hz, 1H), 5.35 (s, 2H), 4.88 (br s, 2H), 3.95 (m, 4H), 2.85 (m, 4H), 2.30 (m, 1H), 1.95 (m, 2H), 1.76 (m, 4H), 1.52 (m, 2H)	482
I-166		2-[2-Amino-5-[4-(4-methyl-piperazine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl]-benzonitrile	3.2	see examples	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.8 Hz,, 1H), 7.76 (d, J = 7.5 Hz, 2H), 7.66 (m, 2H), 7.51 (m, 2H), 7.46 (m, 2H), 7.24(d, J = 1.4 Hz, 1H), 5.35 (s, 2H), 5.01 (br s, 2H), 3.65 (m, 4H), 2.45 (m, 4H), 2.36 (s, 3H)	428
I-167		2-[5-[4-(1-Acetyl-piperazine-1-carbonyl)-phenyl]-3-amino-pyridin-2-yloxymethyl]-benzonitrile	6.7	see examples	(300 MHz, $CDCl_3$) δ 7.95 (d, J = 1.7 Hz,, 1H), 7.76 (d, J = 7.5 Hz, 2H), 7.66 (m, 2H), 7.54 (m, 2H), 7.50 (m, 2H), 7.25(d, J = 1.4 Hz, 1H), 5.35 (s, 2H), 5.27 (br s, 2H), 3.65 (m, 8H), 2.14 (s, 3H)	456
I-168		4-[5-Amino-6-(2-cyano-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide	10.8	see examples	(300 MHz, $CDCl_3$) δ 7.99 (d, J = 1.8 Hz,, 1H), 7.82 (d, J = 8.3 Hz, 2H), 7.74 (m, 1H), 7.66 (m, 2H), 7.55 (m, 3H), 7.25(d, J = 1.8 Hz, 1H), 6.19 (d, J = 8.0 Hz, 1H), 5.35 (s, 2H), 4.88 (br s, 2H), 4.05 (m, 1H), 2.99 (m, 1H), 2.46 (s, 3H), 2.40 (m, 1H), 2.05 (m, 1H), 1.79 (m, 1H), 1.65 (m, 2H), 0.95 (m, 2H)	442
I-169		4-[5-Amino-6-(2-cyano-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide	8.6	see examples	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.8 Hz,, 1H), 7.85 (d, J = 8.4 Hz, 2H), 7.76 (d, J = 7.4 Hz, 1H), 7.66 (m, 2H), 7.57 (m, 3H), 7.27(d, J = 1.8 Hz, 1H), 7.06 (m, 1H), 5.36 (s, 2H), 5.14 (br s, 2H), 3.78 (m, 4H), 3.63 (m, 2H), 2.73 (m, 2H), 2.63 (m, 4H)	485

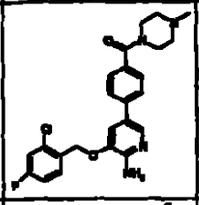
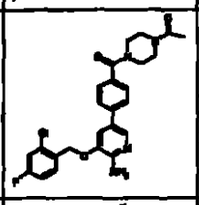
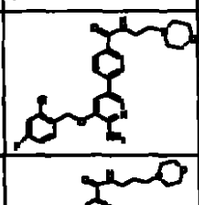
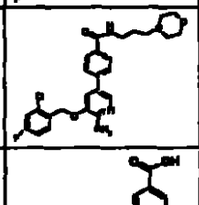
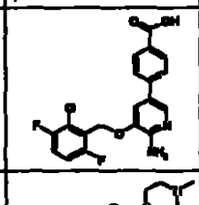
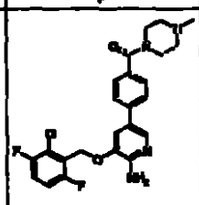
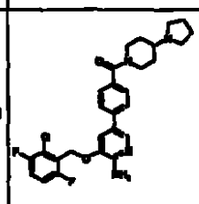
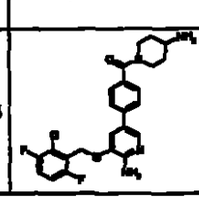
No.	Structure	Name	Met IC$_{50}$ (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-170		4-[6-Amino-5-(2-cyano-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide	17.3	see examples	(300 MHz, $CDCl_3$) δ 8.01 (d, *J* = 1.7 Hz,, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.76 (d, *J* = 7.5 Hz, 1H), 7.57 (m, 1H), 7.58 (d, , *J* = 8.4 Hz, 2H), 7.45 (m, 3H), 7.27(d, *J* = 1.8 Hz, 1H), 6.36 (s, 2H), 4.89 (br s, 2H), 3.74 (m, 4H), 3.60 (m, 2H), 2.57 (m, 6H), 1.82 (m, 2H)	472
I-171		4-[6-Amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid		see examples	(400 MHz, DMSO-d_6) δ 5.35 (s, 2H, CH_2), 5.90 (br s, 2H, NH_2), 7.30-8.00 (multiplets, 6H, aromatic)	389
I-172		{4-[6-Amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.81	see examples	(300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 1.7 Hz, 1H), 7.47 (m, 6H), 7.30 (dd, *J* = 2.0 Hz, *J* = 8.3 Hz, 1H), 7.18(d, *J* = 1.7 Hz, 1H), 5.21 (s, 2H), 4.85 (br s, 2H), 4.42 (m, 1H), 3.60 (m, 2H), 2.64 (m, 4H), 2.2-1.5 (m, 10H)	527
I-173		{4-[6-Amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.66	see examples	(300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 1.7 Hz, 1H), 7.47 (m, 6H), 7.30 (dd, *J* = 2.0 Hz, *J* = 8.3 Hz, 1H), 7.18(d, *J* = 1.7 Hz, 1H), 5.21 (s, 2H), 4.85 (br s, 2H), 4.42 (m, 1H), 3.60 (m, 2H), 2.64 (m, 4H), 2.2-1.5 (m, 10H)	527
I-174		{4-[6-Amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone	0.8	see examples	(300 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.50 (m, 6H), 7.30 (dd, *J* = 1.9 Hz, *J* = 8.3 Hz, 1H), 7.20(s, 1H), 5.21 (s, 2H), 5.07 (br s, 2H), 3.80 (m, 1H), 3.62 (m, 2H), 3.45 (m, 1H), 2.85 (m, 1H), 2.32 (s, 3H), 2.23 (s, 3H), 1.89 (m, 2H)	486
I-175		{4-[6-Amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone	1.2	see examples		458
I-176		{4-[6-Amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.85	see examples	(300 MHz, $CDCl_3$) δ 7.96 (d, *J* = 1.9 Hz, 1H), 7.71 (d, *J* = 3.5 Hz, 1H), 7.50 (m, 5H), 7.30 (dd, *J* = 2.0 Hz, *J* = 8.3 Hz, 1H), 7.18(d, *J* = 1.8 Hz, 1H), 5.22 (s, 2H), 4.83 (br s, 2H), 4.23 (m, 2H), 2.78 (m, 2H), 1.95 (m, 2H), 1.76 (m, 3H), 1.26 (m, 4H), 0.85 (m, 4H)	525

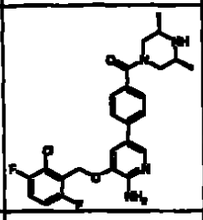
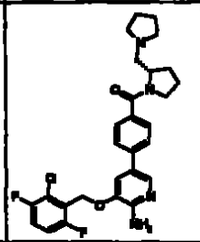
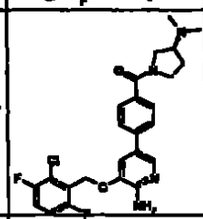
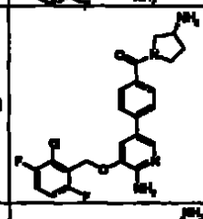
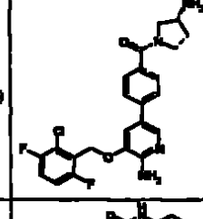
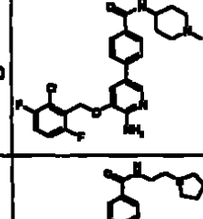
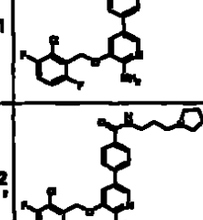
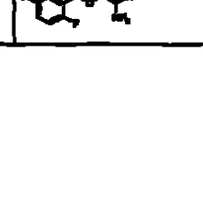
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-177		(4-[6-Amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone	0.79	see examples	(300 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.50 (m, 6H), 7.30 (dd, J = 1.8 Hz, J = 8.3 Hz, 1H), 7.20(s, 1H), 5.21 (s, 2H), 5.07 (br s, 2H), 3.85 (m, 4H), 2.45 (m, 4H), 2.36 (s, 3H)	473
I-178		1-(4-{4-[6-Amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-benzoyl}-piperazin-1-yl)-ethanone	1.67	see examples	(300 MHz, $CDCl_3$) δ 7.97 (d, J = 1.8 Hz, 1H), 7.50 (m, 6H), 7.30 (dd, J = 2.0 Hz, J = 8.3 Hz, 1H), 7.18(d, J = 1.8 Hz, 1H), 5.22 (s, 2H), 4.67 (br s, 2H), 3.84 (m, 4H), 3.53 (m, 4H), 2.14 (s, 3H)	501
I-179		4-[6-Amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide	1.12	see examples	(300 MHz, $CDCl_3$) δ 7.99 (d, J = 1.8 Hz, 1H), 7.81 (d, J = 8.3 Hz, 2H), 7.55 (d, J = 8.3 Hz, 2H), 7.49 (m, 2H), 7.30 (dd, J = 2.0 Hz, J = 8.3 Hz, 1H), 7.18(d, J = 1.8 Hz, 1H), 6.09 (br d, 1H), 5.22 (s, 2H), 4.83 (br s, 2H), 4.05 (m, 1H), 3.06 (m, 1H), 2.48 (s, 3H), 2.32 (m, 1H), 2.12 (m, 1H), 1.89 (m, 1H), 1.28 (m, 2H), 0.88 (m, 2H)	486
I-180		4-[6-Amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide	3.8	see examples	(300 MHz, $CDCl_3$) δ 7.98 (d, J = 1.8 Hz, 1H), 7.84 (d, J = 8.3 Hz, 2H), 7.56 (d, J = 8.3 Hz, 2H), 7.46 (m, 2H), 7.30 (dd, J = 2.0 Hz, J = 8.3 Hz, 1H), 7.20(d, J = 1.8 Hz, 1H), 6.90 (br t, 1H), 5.22 (s, 2H), 4.91 (br s, 2H), 3.75 (m, 4H), 3.59 (m, 2H), 2.65 (m, 2H), 2.55 (m, 4H)	502
I-181		4-[6-Amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide	2	see examples	(300 MHz, $CDCl_3$) δ 7.99 (d, J = 1.7 Hz, 1H), 7.87 (d, J = 8.3 Hz, 2H), 7.71 (m, 1H), 7.55 (d, J = 8.3 Hz, 2H), 7.47 (m, 2H), 7.30 (dd, J = 2.0 Hz, J = 8.3 Hz, 1H), 7.21 (d, J = 1.7 Hz, 1H), 6.23 (s, 2H), 4.91 (br s, 2H), 3.75 (m, 4H), 3.59 (m, 2H), 2.60 (m, 6H), 1.83 (m, 2H)	516
I-182		4-[6-Amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-benzoic acid		see examples	(400 MHz, DMSO-d_6) δ 5.35 (s, 2H, CH_2), 5.95 (br s, 2H, NH_2), 7.40 - 8.00 (multiplet, 10H, aromatic)	388 (M+)
I-183		(4-[6-Amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl)-[(2*R*)-3-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.75	see examples	^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, J = 1.7 Hz, 1H), 7.74 (d, J = 7.8 Hz, 1H), 7.68 (d, J = 7.7 Hz, 1H), 7.53 (m, 6H), 7.15 (d, J = 1.7 Hz, 1H), 5.35 (s, 2H), 4.82 (br s, 2H), 4.42 (m, 1H), 3.50 (m, 2H), 2.65 (m, 4H), 2.2-1.5 (m, 10H)	525

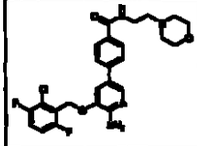
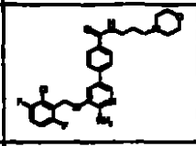
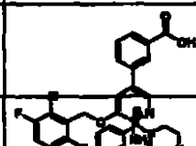
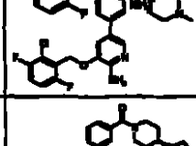
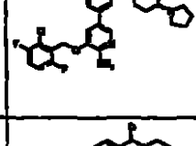
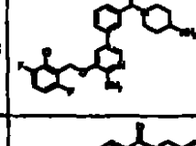
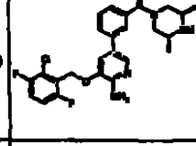
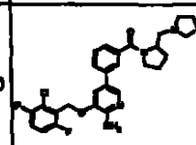
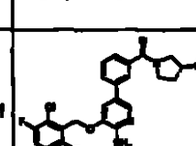
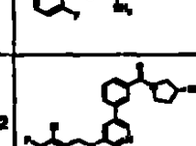
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-184		(4-[6-Amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl)-[(2S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	>20	see examples	(300 MHz, $CDCl_3$) δ 7.86 (d, J = 1.7 Hz, 1H), 7.74 (d, J = 7.8 Hz, 1H), 7.68 (d, J = 7.7 Hz, 1H), 7.53 (m, 6H), 7.15 (d, J = 1.7 Hz, 1H), 5.35 (s, 2H), 4.82 (br s, 2H), 4.42 (m, 1H), 3.50 (m, 2H), 2.65 (m, 4H), 2.2-1.5 (m, 10H)	525
I-185		(4-[6-Amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl)-[(3S)-3-dimethylamino-pyrrolidin-1-yl]-methanone	1.39	see examples	(300 MHz, $CDCl_3$) δ 7.87 (d, J = 2.1 Hz, 1H), 7.74 (d, J = 7.8 Hz, 1H), 7.68 (d, J = 7.7 Hz, 1H), 7.51 (m, 6H), 7.16 (d, J = 2.1 Hz, 1H), 5.35 (s, 2H), 4.88 (br s, 2H), 3.89 (m, 1H), 3.65 (m, 2H), 3.45 (m, 1H), 2.78 (m, 1H), 2.31 (s, 3H), 2.22 (s, 3H), 2.11 (m, 1H), 1.89 (m, 1H).	485
I-186		[(3S)-3-Amino-pyrrolidin-1-yl]-(4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl)-methanone	0.79	see examples	(300 MHz, $CDCl_3$) δ 7.83 (d, J = 1.4 Hz, 1H), 7.74 (d, J = 7.7 Hz, 1H), 7.67 (d, J = 7.4 Hz, 1H), 7.55 (m, 3H), 7.46 (m, 3H), 7.15 (d, J = 1.4 Hz, 1H), 5.36 (s, 2H), 5.01 (br s, 2H), 3.85 (m, 4H), 2.03 (m, 3H), 1.78 (m, 1H), 0.85 (m, 1H)	457
I-187		(4-[6-Amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	1.01	see examples	(300 MHz, $CDCl_3$) δ 7.86 (d, J = 1.8 Hz, 1H), 7.74 (d, J = 7.9 Hz, 1H), 7.68 (m, 1H), 7.60 (m, 1H), 7.47 (m, 6H), 7.14 (d, J = 1.9 Hz, 1H), 5.35 (s, 2H), 4.81 (br s, 2H), 4.60 (m, 1H), 3.74 (m, 1H), 2.96 (m, 2H), 2.65 (m, 2H), 2.22 (m, 1H), 1.85 (m, 2H), 1.65 (m, 4H), 1.25 (m, 2H), 0.96 (m, 2H)	525
I-188		(4-[6-Amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone	1.61	see examples	(300 MHz, $CDCl_3$) δ 7.86 (d, J = 1.8 Hz, 1H), 7.74 (d, J = 7.7 Hz, 1H), 7.68 (d, J = 7.7 Hz, 1H), 7.60 (t, J = 7.7 Hz, 1H), 7.48 (m, 6H), 7.14 (d, J = 1.8 Hz, 1H), 5.35 (s, 2H), 4.89 (br s, 2H), 3.80 (m, 2H), 3.51 (m, 2H), 2.40 (m, 4H), 2.32 (s, 3H)	471
I-189		1-(4-[4-[6-Amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-benzoyl)-piperazin-1-yl)-ethanone	6.7	see examples	(300 MHz, $CDCl_3$) δ 7.86 (d, J = 1.8 Hz, 1H), 7.74 (d, J = 7.7 Hz, 1H), 7.68 (d, J = 7.7 Hz, 1H), 7.60 (t, J = 7.7 Hz, 1H), 7.48 (m, 6H), 7.14 (d, J = 1.8 Hz, 1H), 5.36 (s, 2H), 4.87 (br s, 2H), 3.84 (m, 4H), 3.53 (m, 4H), 2.14 (s, 3H)	499
I-190		4-[6-Amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-N'-(1-methyl-piperidin-4-yl)-benzamide	3.8	see examples	(300 MHz, $CDCl_3$) δ 7.86 (d, J = 1.8 Hz, 1H), 7.79 (d, J = 8.3 Hz, 2H), 7.74 (d, J = 7.8 Hz, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.60 (m, 1H), 7.52 (m, 3H), 7.14 (d, J = 1.8 Hz, 1H), 5.96 (m, 1H), 5.36 (s, 2H), 4.85 (br s, 2H),), 4.05 (m, 1H), 2.80 (m, 2H), 2.32 (s, 3H), 2.16 (m, 2H), 2.01 (m, 2H), 1.62 (m, 2H)	485
I-191		4-[6-Amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-N'-(2-morpholin-4-yl-ethyl)-benzamide	8.2	see examples	(300 MHz, $CDCl_3$) δ 7.86 (d, J = 1.8 Hz, 1H), 7.82 (d, J = 8.4 Hz, 2H), 7.74 (d, J = 7.8 Hz, 1H), 7.68 (d, J = 7.7 Hz, 1H), 7.60 (t, , J = 7.7 Hz, 1H), 7.53 (m, 3H), 7.17 (d, J = 1.8 Hz, 1H), 6.83 (m, 1H), 5.36 (s, 2H), 4.89 (br s, 2H), 3.74 (m, 4H), 3.57 (m, 2H), 2.62 (m, 2H), 2.52 (m, 4H)	501

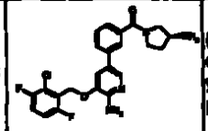
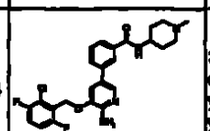
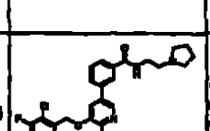
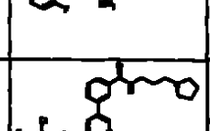
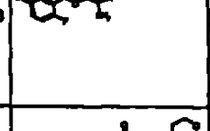
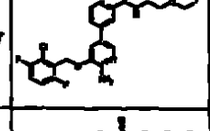
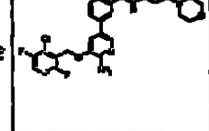
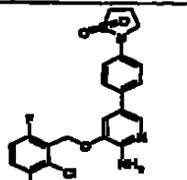
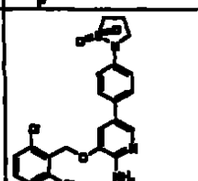
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-192		4-[6-Amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide	3.8	see examples	(300 MHz, $CDCl_3$) δ 7.98 (d, *J* = 1.8 Hz, 1H), 7.86 (m, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.74 (d, *J* = 7.7 Hz, 1H), 7.68 (d, *J* = 7.7 Hz, 1H), 7.60 (t, *J* = 7.7 Hz, 1H), 7.53 (m, 3H), 7.17 (d, *J* = 1.8 Hz, 1H), 6.38 (s, 2H), 4.94 (br s, 2H), 3.75 (m, 4H), 3.59 (m, 2H), 2.59 (m, 6H), 1.83 (m, 2H)	615
I-193		4-[6-Amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-benzoic acid		see examples	(400 MHz, DMSO-d_6) δ 1.29 (s, 9H, t-butyl), 5.20 (s, 2H, CH_2), 6.95 (br s, 2H, NH_2), 7.35-8.00 (multiplets, 10H, aromatic)	376 (M+)
I-194		(4-[6-Amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-phenyl)-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	1.89	see examples	(300 MHz, $CDCl_3$) δ 7.94 (d, *J* = 1.7 Hz, 1H), 7.48 (m, 6H), 7.21 (d, *J* = 1.7 Hz, 1H), 6.11 (s, 2H), 4.80 (br s, 2H), 4.48 (m, 1H), 3.48 (m, 2H), 2.62 (m, 4H), 2.2-1.5 (m, 10H), 1.34 (s, 9H)	513
I-195		(4-[6-Amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-phenyl)-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	3.27	see examples	(300 MHz, $CDCl_3$) δ 7.94 (d, *J* = 1.7 Hz, 1H), 7.48 (m, 6H), 7.21 (d, *J* = 1.7 Hz, 1H), 6.11 (s, 2H), 4.80 (br s, 2H), 4.48 (m, 1H), 3.48 (m, 2H), 2.62 (m, 4H), 2.2-1.5 (m, 10H), 1.34 (s, 9H)	513
I-196		(4-[6-Amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-phenyl)-[(3*R*)-3-dimethylamino-pyrrolidin-1-yl]-methanone	4.29	see examples	(300 MHz, $CDCl_3$) δ 7.94 (d, *J* = 2.1 Hz, 1H), 7.54 (m, 4H), 7.48 (d, *J* = 8.3 Hz, 2H), 7.38 (d, *J* = 8.3 Hz, 2H), 7.21 (d, *J* = 1.7 Hz, 1H), 6.11 (s, 2H), 4.84 (br s, 2H), 3.89 (m, 1H), 3.84 (m, 2H), 3.42 (m, 1H), 2.70 (m, 1H), 2.31 (s, 3H), 2.22 (s, 3H), 2.05 (m, 1H), 1.89 (m, 1H), 1.34 (s, 9H)	473
I-197		(4-[6-Amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone	3.8	see examples	(300 MHz, $CDCl_3$) δ 7.93 (d, *J* = 1.7 Hz, 1H), 7.48 (m, 4H), 7.41 (m, 4H), 7.21 (d, *J* = 1.7 Hz, 1H), 6.11 (s, 2H), 4.85 (br s, 2H), 3.80 (m, 2H), 3.62 (m, 2H), 2.41 (m, 4H), 2.33 (s, 3H), 1.34 (s, 9H)	459
I-198		1-(4-{4-[6-Amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-benzoyl}-piperazin-1-yl)-ethanone	3	see examples	(300 MHz, $CDCl_3$) δ 7.94 (d, *J* = 1.8 Hz, 1H), 7.50 (m, 6H), 7.21 (d, *J* = 1.7 Hz, 1H), 6.11 (s, 2H), 4.80 (br s, 2H), 3.84 (m, 4H), 3.63 (m, 4H), 2.14 (s, 3H), 1.34 (s, 9H)	487
I-199		4-[6-Amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide	2.82	see examples	(300 MHz, $CDCl_3$) δ 7.95 (d, *J* = 1.8 Hz, 1H), 7.80 (d, *J* = 8.3 Hz, 2H), 7.54 (d, *J* = 8.3 Hz, 2H), 7.44 (d, *J* = 7.7 Hz, 2H), 7.38 (d, *J* = 7.7 Hz, 2H), 7.21 (d, *J* = 1.8 Hz, 1H), 6.05 (m, 1H), 6.11 (s, 2H), 4.80 (br s, 2H), 4.01 (m, 1H), 2.84 (m, 2H), 2.33 (s, 3H), 2.20 (m, 2H), 2.10 (m, 2H), 1.82 (m, 2H), 1.34 (s, 9H)	487

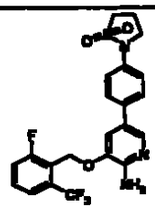
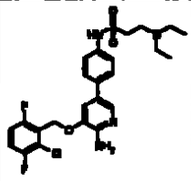
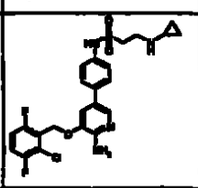
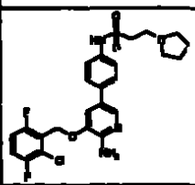
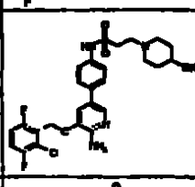
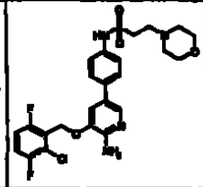
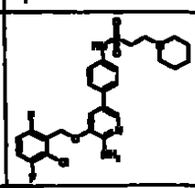
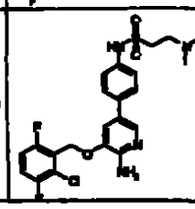
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-200		4-[6-Amino-5-(4-tert-butyl-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide	6.85	see examples	(300 MHz, $CDCl_3$) δ 7.95 (d, *J* = 1.8 Hz, 1H), 7.82 (d, *J* = 8.3 Hz, 2H), 7.64 (d, *J* = 8.3 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 1.8 Hz, 1H), 6.91 (t, *J* = 4.6 Hz, 1H), 5.10 (s, 2H), 4.90 (br s, 2H), 3.74 (m, 4H), 3.57 (m, 2H), 2.62 (m, 2H), 2.51 (m, 4H), 1.34 (s, 9H)	488
I-201		4-[6-Amino-5-(4-tert-butyl-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide	8.3	see examples	(300 MHz, $CDCl_3$) δ 8.01 (t, J = 4.5 Hz, 1H), 7.86 (d, *J* = 1.8 Hz, 1H), 7.88 (d, *J* = 8.3 Hz, 2H), 7.64 (d, *J* = 8.3 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 1.8 Hz, 1H), 5.12 (s, 2H), 4.89 (br s, 2H), 3.74 (m, 4H), 3.59 (m, 2H), 2.58 (m, 6H), 1.82 (m, 2H), 1.34 (s, 9H)	503
I-202		4-[6-Amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-benzoic acid		see examples	(400 MHz, DMSO-d_6) δ 5.25 (s, 2H, CH_2), 5.80 (br s, 2H, NH_2), 7.20 - 8.00 (multiplets, 6H, aromatic)	374
I-203		(4-[6-Amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-phenyl)-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	1.48	see examples	(300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 1.7 Hz, 1H), 7.82 (m, 6H), 7.20 (m, 1H), 7.05 (m, 1H), 6.21 (s, 2H), 4.80 (br s, 2H), 4.45 (m, 1H), 3.62 (m, 2H), 2.78 (m, 4H), 2.2-1.5 (m, 10H)	509
I-204		(4-[6-Amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-phenyl)-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	2.5	see examples	(300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 1.7 Hz, 1H), 7.82 (m, 6H), 7.20 (m, 1H), 7.05 (m, 1H), 6.21 (s, 2H), 4.80 (br s, 2H), 4.45 (m, 1H), 3.62 (m, 2H), 2.78 (m, 4H), 2.2-1.5 (m, 10H)	509
I-205		(4-[6-Amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-phenyl)-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone	6.1	see examples	(300 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.82 (m, 6H), 7.20 (m, 1H), 7.04 (m, 1H), 6.21 (s, 2H), 4.95 (br s, 2H), 3.90 (m, 1H), 3.61 (m, 2H), 3.33 (m, 1H), 2.75 (m, 1H), 2.32 (s, 3H), 2.23 (s, 3H), 2.10 (m, 1H), 1.89 (m, 1H)	469
I-206		(4-[6-Amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-phenyl)-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone	1.83	see examples	(300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 1.8 Hz, 1H), 7.82 (m, 6H), 7.20 (m, 1H), 7.04 (m, 1H), 6.21 (s, 2H), 4.84 (br s, 2H), 3.84 (m, 4H), 2.16 (m, 1H), 1.76 (m, 2H), 1.56 (m, 2H)	441

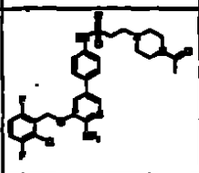
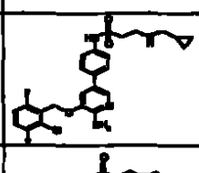
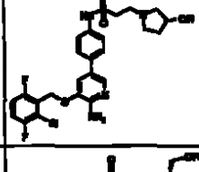
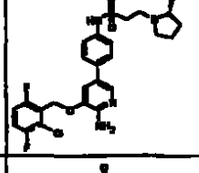
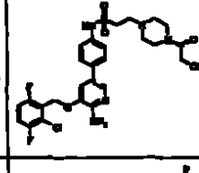
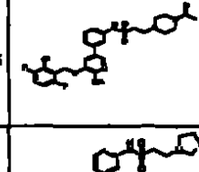
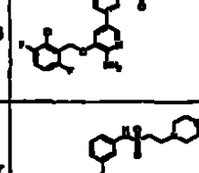
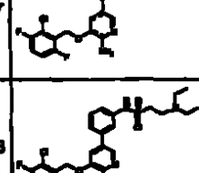
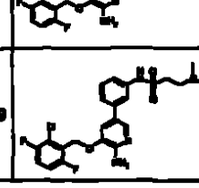
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-207		(4-[6-Amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone	5	see examples	(300 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.52 (m, 6H), 7.20 (m, 1H), 7.04 (m, 1H), 5.21 (s, 2H), 4.89 (br s, 2H), 3.80 (m, 2H), 3.65 (m, 2H), 2.43 (m, 4H), 2.23 (s, 3H)	458
I-208		1-(4-{4-[6-Amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-benzoyl}-piperazin-1-yl)-ethanone	5.3	see examples	(300 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.52 (m, 6H), 7.20 (m, 1H), 7.04 (m, 1H), 5.21 (s, 2H), 4.90 (br s, 2H), 3.87 (m, 4H), 3.53 (m, 4H), 2.22 (s, 3H)	483
I-209		4-[6-Amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide	11	see examples	(300 MHz, $CDCl_3$) δ 7.99 (d, *J* = 1.8 Hz, 1H), 7.84 (d, *J* = 8.3 Hz, 2H), 7.57 (d, *J* = 8.3 Hz, 2H), 7.49 (dd, *J* = 8.0 Hz, 8.5 Hz, 1H), 7.20 (m, 2H), 7.04 (m, 1H), 6.82 (m, 1H), 5.22 (s, 2H), 4.85 (br s, 2H), 3.74 (m, 4H), 3.66 (m, 2H), 2.63 (m, 2H), 2.53 (m, 4H)	485
I-210		4-[6-Amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide	5.8	see examples	(300 MHz, $CDCl_3$) δ 8.06 (m, 1H), 7.00 (d, *J* = 1.8 Hz, 1H), 7.89 (d, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.49 (dd, *J* = 8.0 Hz, 8.5 Hz, 1H), 7.20 (m, 2H), 7.04 (m, 1H), 5.22 (s, 2H), 4.85 (br s, 2H), 3.75 (m, 4H), 3.60 (m, 2H), 2.55 (m, 6H), 1.83 (m, 2H)	499
I-211		4-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid	0.35	see examples	(300 MHz, DMSO-d_6) δ 5.21 (s, 2H), 5.71 (s, 2H), 7.31-7.46 (m, 1H), 7.5-7.82 (m, 4H), 7.91-7.94 (m, 3H).	
I-212		(4-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone	0.093	see examples	(300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 1.6 Hz, 1H), 7.56 (d, *J* = 8.2 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 1.8 Hz, 1H), 7.20 (m, 1H), 7.06 (m, 1H), 5.29 (s, 2H), 4.81 (br s, 2H), 3.79 (m, 2H), 3.64 (m, 2H), 2.44 (m, 4H), 2.33 (s, 3H)	473
I-213		(4-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.049	see examples	(300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 1.7 Hz, 1H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.45 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 1.8 Hz, 1H), 7.20 (m, 1H), 7.06 (m, 1H), 5.29 (s, 2H), 4.79 (br s, 2H), 4.60 (m, 1H), 3.85 (m, 1H), 3.02 (m, 2H), 2.65 (m, 4H), 2.36 (m, 1H), 2.06 (m, 4H), 1.86 (m, 4H).	527
I-214		(4-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-(4-amino-piperidin-1-yl)-methanone	0.1	see examples	(400 MHz, DMSO-d_6) δ 7.82 (s, 1H), 7.66 (m, 4H), 7.46 (m, 4H), 5.89 (s, 2H), 5.39 (s, 2H), 4.19 (m, 1H), 3.60 (m, 2H), 2.64 (m, 6H), 1.86 (m, 2H), 1.63 (m, 3H), 1.54 (m, 4H)	MS (ESI+) m/z 543 (MH+). MS m/z 473 [M+1]

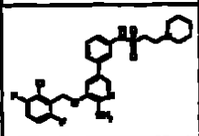
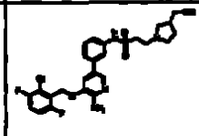
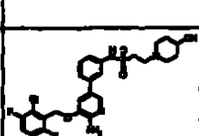
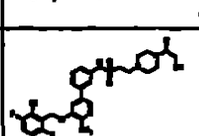
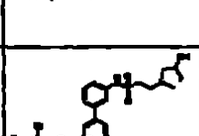
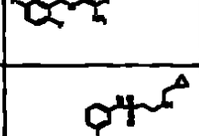
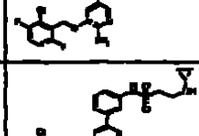
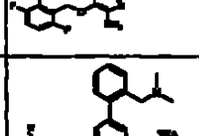
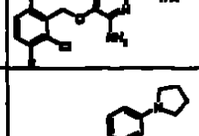
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-215		(4-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-(3,5-dimethyl-piperazin-1-yl)-methanone	0.1	see examples	(400 MHz, DMSO-d_6) δ 7.96 (s, 1H), 7.56 (d, 2H), 7.41 (d, 2H), 7.31 (s, 1H), 7.19 (m, 1H), 7.08 (m, 1H), 6.31 (s, 2H), 4.81 (m, 2H), 4.66 (m, 1H), 3.69 (m, 1H), 2.89 (m, 2H), 2.69 (m, 1H), 2.40 (m, 1H), 1.74 (m, 1H), 1.18 (d, 6H)	467
I-216		(4-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-[(2S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.1	see examples	(400MHz, DMSO-d_6) δ 7.95 (d, 1H), 7.69 (d, 2H), 7.58 (m, 2H), 7.50 (d, 2H), 7.40 (m, 1H), 5.81 (s, 2H), 5.29 (s, 2H), 4.35 (m, 1H), 3.5 (d, 2H), 2.87 (d, 2H), 2.71 (d, 2H), 1.7-2.0 (m, 10H)	527
I-217		(4-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-[(3S)-3-dimethylamino-pyrrolidin-1-yl]-methanone	0.12	see examples	(400 MHz, DMSO-d_6) δ 7.97 (s, 1H), 7.80 (m, 4H), 7.32 (s, 1H), 7.18 (m, 1H), 7.04 (m, 1H), 5.31 (s, 2H), 4.78 (m, 2H), 3.90 (m, 1H), 3.69 (m, 2H), 3.41 (m, 1H), 2.78 (m, 1H), 2.31 (s, 3H), 2.24 (s, 3H), 2.08 (m, 1H), 1.84 (m, 1H)	467
I-218		(4-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-[(3R)-3-amino-pyrrolidin-1-yl]-methanone	0.053	see examples	(400 MHz, DMSO-d_6) δ 7.84 (s, 1H), 7.62 (m, 5H), 7.35 (m, 1H), 7.20 (m, 1H), 5.38 (s, 2H), 3.78 (m, 3H), 3.55 (m, 1H), 3.41 (m, 1H), 2.18 (m, 1H), 1.82 (m, 1H)	459
I-219		(4-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-[(3S)-3-amino-pyrrolidin-1-yl]-methanone	0.085	see examples	(400 MHz, DMSO-d_6) δ 7.84 (s, 1H), 7.62 (m, 5H), 7.35 (m, 1H), 7.20 (m, 1H), 5.38 (s, 2H), 3.78 (m, 3H), 3.55 (m, 1H), 3.41 (m, 1H), 2.18 (m, 1H), 1.82 (m, 1H)	459
I-220		4-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide	0.11	see examples	(400 MHz, DMSO-d_6) δ 7.97 (s, 1H), 7.80 (d, 2H), 7.66 (d, 2H), 7.36 (s, 1H), 7.18 (m, 1H), 7.04 (m, 1H), 6.01 (d, 1H), 5.28 (s, 2H), 4.78 (s, 2H), 3.98 (m, 1H), 2.85 (m, 2H), 2.31 (s, 3H), 2.18 (t, 2H), 2.10 (m, 2H), 1.65 (m, 2H)	467
I-221		4-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(2-pyrrolidin-1-yl-ethyl)-benzamide	0.16	see examples	(400 MHz, DMSO-d_6) δ 7.98 (s, 1H), 7.89 (d, 2H), 7.56 (d, 2H), 7.45 (m, 1H), 7.31 (s, 1H), 7.17 (m, 1H), 7.01 (m, 1H), 5.28 (s, 2H), 4.85 (s, 2H), 3.65 (m, 2H), 2.89 (t, 2H), 2.78 (m, 4H), 1.89 (m, 4H)	467
I-222		4-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(3-pyrrolidin-1-yl-propyl)-benzamide	0.16	see examples	(400 MHz, DMSO-d_6) δ 8.72 (m, 1H), 7.95 (m, 3H), 7.57 (d, 2H), 7.35 (s, 1H), 7.18 (m, 1H), 7.02 (m, 1H), 5.31 (s, 2H), 4.79 (s, 2H), 3.88 (m, 2H), 2.89 (m, 6H), 1.97 (m, 6H)	501

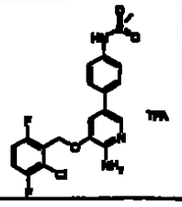
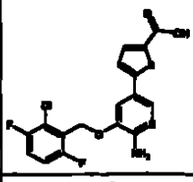
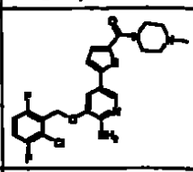
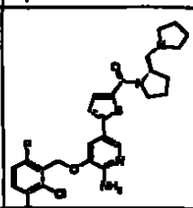
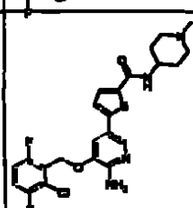
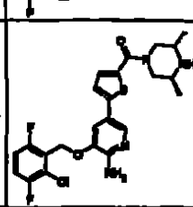
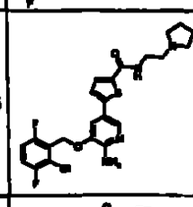
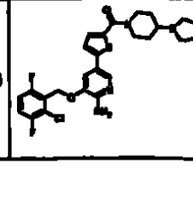
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-223		4-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide	0.166	see examples	(400 MHz, DMSO-d_6) δ 7.97 (s, 1H), 7.82 (d, 2H), 7.62 (d, 2H), 7.39 (s, 1H), 7.18 (m, 1H), 7.05 (m, 1H), 6.81 (m, 1H), 5.28 (s, 2H), 4.79 (s, 2H), 3.76 (m, 4H), 3.58 (m, 2H), 2.63 (t, 2H), 2.61 (m, 4H)	503
I-224		4-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide	0.26	see examples	(400 MHz, DMSO-d_6) δ 8.04 (m, 1H), 7.96 (s, 1H), 7.89 (d, 2H), 7.58 (d, 2H), 7.38 (s, 1H), 7.18 (m, 1H), 7.06 (m, 1H), 7.29 (s, 2H), 4.81 (s, 2H), 3.76 (m, 4H), 3.61 (m, 2H), 2.59 (t, 2H), 2.54 (m, 4H), 1.79 (m, 2H)	517
I-225		3-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid	3.7/0.6	see examples	(300 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.92 (s, 1H), 7.84 (d, *J* = 7.4 Hz, 1H), 7.60 (m, 2H), 7.55 (s, 1H), 7.40 (m, 2H), 6.75 (s, 2H), 5.31 (br s, 2H)	391
I-226		(3-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone	0.066	see examples	(300 MHz, $CDCl_3$) δ 7.96 (d, *J* = 1.7 Hz, 1H), 7.58 (dd, *J* = 1.1 Hz, 6.8 Hz, 1H), 7.46 (m, 1H), 7.35 (m, 3H), 7.20 (m, 1H), 7.06 (m, 1H), 6.27 (s, 2H), 4.81 (br s, 2H), 3.63 (m, 2H), 3.50 (m, 2H), 2.49 (m, 2H), 2.39 (m, 2H), 2.33 (s, 3H)	473
I-227		(3-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.05	see examples	(300 MHz, $CDCl_3$) δ 7.96 (d, *J* = 1.8 Hz, 1H), 7.57 (dd, *J* = 1.2 Hz, 8.0 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.34 (m, 3H), 7.20 (m, 1H), 7.06 (m, 1H), 6.27 (s, 2H), 4.77 (br s, 2H), 4.60 (m, 1H), 3.80 (m, 1H), 3.02 (m, 2H), 2.80 (m, 2H), 2.39 (m, 1H), 1.98 (m, 2H), 1.85 (m, 4H), 1.65 (m, 4H)	527
I-228		(3-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-(4-amino-piperidin-1-yl)-methanone	0.23	see examples	(300 MHz, CD_3OD) δ 8.01 (s, 1H), 7.89 (s, 1H), 7.76 (m, 2H), 7.59 (s, 1H), 7.48 (t, 1H), 7.31 (m, 1H), 7.18 (m, 1H), 6.38 (s, 2H), 4.01 (m, 1H), 3.09 (m, 2H), 2.68 (t, 2H), 1.97 (m, 2H), 1.39 (m, 2H)	473
I-229		(3-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-(3,5-dimethyl-piperazin-1-yl)-methanone	0.068/ 0.18	see examples	(300 MHz, $CDCl_3$) δ 7.96 (d, *J* = 1.7 Hz, 1H), 7.56 (m, 1H), 7.47 (t, *J* = 7.8 Hz, 1H), 7.36 (m, 3H), 7.20 (m, 1H), 7.06 (m, 1H), 6.27 (s, 2H), 4.62 (br s, 2H), 4.02 (m, 1H), 3.65 (m, 1H), 3.30 (m, 2H), 2.70 (m, 1H), 2.40 (m, 1H), 1.97 (m, 1H), 1.15 (d, 3H), 0.99 (d, 3H)	487
I-230		(3-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-[(2S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.19	see examples	(300 MHz, $CDCl_3$) δ 7.96 (d, *J* = 1.7 Hz, 1H), 7.66 (s, 1H), 7.57 (d, *J* = 6.8 Hz, 1H), 7.45 (m, 2H), 7.36 (d, *J* = 1.7 Hz, 1H), 7.20 (m, 1H), 7.06 (m, 1H), 6.27 (s, 2H), 4.78 (br s, 2H), 4.42 (m, 1H), 3.46 (m, 2H), 2.66 (m, 4H), 2.2-1.5 (m, 10H)	527
I-231		(3-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-[(2*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone	0.128	see examples	(300 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.68 (d, *J* = 7.4 Hz, 1H), 7.59 (m, 1H), 7.44 (m, 2H), 7.36 (s, 1H), 7.20 (m, 1H), 7.06 (m, 1H), 6.27 (s, 2H), 4.80 (br s, 2H), 3.90 (m, 1H), 3.61 (m, 2H), 3.41 (m, 1H), 2.77 (m, 1H), 2.32 (s, 3H), 2.22 (s, 3H), 2.10 (m, 1H), 1.82 (m, 1H)	487
I-232		(3-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-[(3*R*)-3-amino-pyrrolidin-1-yl]-methanone	0.12	see examples	(300 MHz, CD_3OD) δ 7.88 (s, 1H), 7.75 (m, 2H), 7.58 (m, 3H), 7.36 (m, 1H), 7.22 (m, 1H), 6.38 (s, 2H), 4.00-3.56 (m, 5H), 2.40 (m, 1H), 2.12 (m, 1H)	459

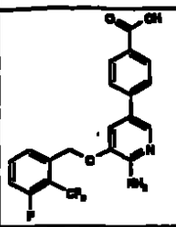
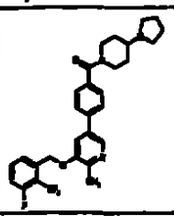
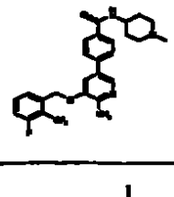
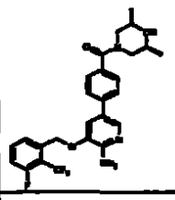
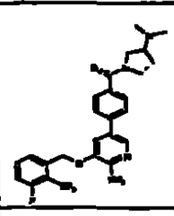
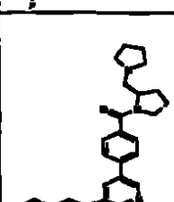
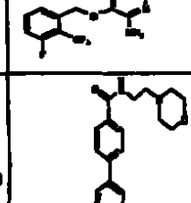
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-233		(3-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl)-[(3S)-amino-pyrrolidin-1-yl]-methanone	0.12	see examples	(300 MHz, CD_3OD) δ 7.86 (s, 1H), 7.75 (m, 2H), 7.58 (m, 3H), 7.38 (m, 1H), 7.22 (m, 1H), 5.38 (s, 2H), 4.00-3.88 (m, 5H), 2.40 (m, 1H), 2.12 (m, 1H).	459
I-234		3-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide	0.23	see examples	(300 MHz, $CDCl_3$) δ 7.96 (d, *J* = 1.7 Hz, 1H), 7.94 (s, 1H), 7.84 (m, 2H), 7.47 (t, *J* = 7.7 Hz, 1H), 7.37 (d, *J* = 1.7 Hz, 1H), 7.20 (m, 1H), 7.06 (m, 1H), 6.26 (m, 1H), 5.27 (s, 2H), 4.81 (br s, 2H), 3.99 (m, 1H), 2.84 (m, 2H), 2.30 (s, 3H), 2.18 (m, 2H), 2.04 (m, 2H), 1.84 (m, 2H)	487
I-235		3-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(2-pyrrolidin-1-yl-ethyl)-benzamide	0.28	see examples	(300 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.96 (d, *J* = 1.7 Hz, 1H), 7.72 (d, *J* = 7.7 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 1H), 7.40 (d, *J* = 1.7 Hz, 1H), 7.20 (m, 2H), 7.06 (m, 1H), 5.27 (s, 2H), 4.83 (br s, 2H), 3.61 (m, 2H), 2.77 (m, 2H), 2.62 (m, 4H), 1.81 (m, 4H)	487
I-236		3-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(3-pyrrolidin-1-yl-propyl)-benzamide	0.28	see examples	(300 MHz, $CDCl_3$) δ 8.78 (m, 1H), 8.04 (d, *J* = 1.8 Hz, 1H), 7.98 (d, *J* = 1.8 Hz, 1H), 7.88 (d, *J* = 7.7 Hz, 1H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 1H), 7.40 (d, *J* = 1.8 Hz, 1H), 7.20 (m, 1H), 7.06 (m, 1H), 5.29 (s, 2H), 4.77 (br s, 2H), 3.61 (m, 2H), 2.77 (m, 2H), 2.66 (m, 4H), 1.87 (m, 2H), 1.80 (m, 4H)	501
I-237		3-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide	0.36	see examples	(300 MHz, $CDCl_3$) δ 7.99 (t, *J* = 1.8 Hz, 1H), 7.97 (d, *J* = 1.8 Hz, 1H), 7.86 (m, 2H), 7.49 (t, *J* = 7.7 Hz, 1H), 7.38 (d, *J* = 1.8 Hz, 1H), 7.20 (m, 1H), 7.06 (m, 2H), 5.27 (s, 2H), 4.85 (br s, 2H), 3.72 (m, 4H), 3.59 (m, 2H), 2.63 (m, 2H), 2.52 (m, 4H)	503
I-238		3-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide	0.35	see examples	(300 MHz, $CDCl_3$) δ 8.02 (m, 2H), 7.97 (d, *J* = 1.8 Hz, 1H), 7.86 (d, *J* = 7.8 Hz, 1H), 7.83 (d, *J* = 8.3 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 1H), 7.38 (d, *J* = 1.8 Hz, 1H), 7.19 (m, 1H), 7.06 (m, 1H), 5.27 (s, 2H), 4.81 (br s, 2H), 3.66 (m, 4H), 3.50 (m, 2H), 2.55 (m, 2H), 2.49 (m, 4H), 1.81 (m, 2H)	517
I-239		*N*-[2-(4-Acetyl-piperazin-1-yl)-ethyl]-3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzamide	0.1	see examples	(300 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.86 (s, 1H), 7.67 (dd, 2H), 7.56 (t, 1H), 7.48 (s, 1H), 7.21 (m, 1H), 7.06 (m, 1H), 6.02 (br s, 2H), 5.39 (s, 2H), 3.75 (m, 4H), 3.60 (m, 2H), 2.79 (m, 2H), 2.60 (m, 4H), 2.11 (s, 3H)	544
I-240		3-(2-Chloro-3,6-difluoro-benzyloxy)-5-[4-(1,1-dioxo-1λ^6-isothiazolidin-2-yl)-phenyl]-pyridin-2-ylamine	0.1	see examples	(400 MHz, DMSO-d_6) δ 7.98 (s, 1H), 7.82 (d, 2H), 7.58 (m, 1H), 7.51 (s, 1H), 7.40 (m, 1H), 7.23 (d, 2H), 6.70 (s, 2H), 5.28 (s, 2H), 3.76 (t, 2H), 3.49 (t, 2H), 2.41 (t, 2H)	466
I-241		3-(2,6-Dichloro-benzyloxy)-5-[4-(1,1-dioxo-1λ^6-isothiazolidin-2-yl)-phenyl]-pyridin-2-ylamine	0.087	see examples		484

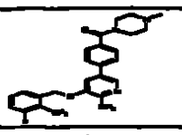
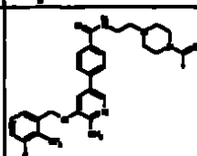
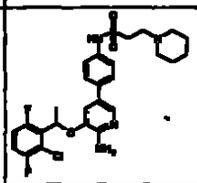
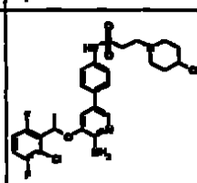
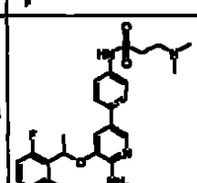
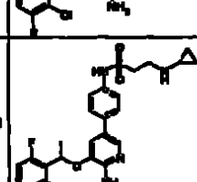
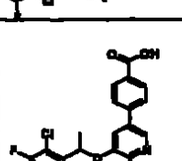
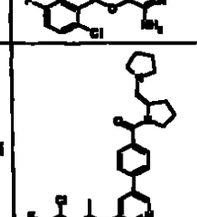
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-242		5-[4-(1,1-Dioxo-1λ^6-isothiazolidin-2-yl)-phenyl]-3-(2-fluoro-6-trifluoromethyl-benzyloxy)-pyridin-2-ylamine	0.14	see examples		482
I-243		2-Diethylamino-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide	0.043	see examples	(300 MHz, $CDCl_3$) δ 7.92 (d, J = 1.8 Hz, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 1.8 Hz, 1H), 7.24 (m, 3H), 7.20 (m, 1H), 7.07 (m, 1H), 5.28 (s, 2H), 4.70 (br s, 2H), 3.22 (t, J = 6.1 Hz, 2H), 3.04 (t, J = 6.1 Hz, 2H), 2.66 (q, J = 7.1 Hz, 4H), 1.10 (t, J = 7.1 Hz, 6H)	625
I-244		2-Cyclopropylamino-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide	0.091	see examples	(300 MHz, $CDCl_3$) δ 7.92 (d, J = 1.8 Hz, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 1.8 Hz, 1H), 7.24 (m, 3H), 7.20 (m, 1H), 7.07 (m, 1H), 5.28 (s, 2H), 4.78 (br s, 2H), 3.25 (s, 4H), 2.17 (m, 1H), 0.9 (m, 1H), 0.80 (m, 2H), 0.40 (m, 2H)	609
I-245		2-Pyrrolidin-1-yl-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide	0.082	see examples	(300 MHz, $CDCl_3$) δ 7.92 (d, J = 1.8 Hz, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7.31 (d, J = 1.5 Hz, 1H), 7.24 (m, 3H), 7.20 (m, 1H), 7.07 (m, 1H), 5.28 (s, 2H), 4.72 (br s, 2H), 3.27 (m, 2H), 3.06 (m, 2H), 2.69 (m, 4H), 1.86 (m, 4H)	523
I-246		2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide	0.135	see examples	(300 MHz, $CDCl_3$) δ 7.92 (d, J = 1.8 Hz, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7.32 (m, 2H), 7.24 (m, 2H), 7.20 (m, 1H), 7.07 (m, 1H), 5.28 (s, 2H), 4.74 (br s, 2H), 3.81 (m, 1H), 3.31 (t, 2H), 2.98 (t, 2H), 2.65 (m, 2H), 2.32 (m, 2H), 1.88 (m, 2H), 1.58 (m, 2H)	553
I-247		2-Morpholin-4-yl-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide	0.31	see examples	(300 MHz, DMSO-d_6) δ 9.80 (br s, 1H), 7.89 (d, J = 1.5 Hz, 1H), 7.69 (m, 3H), 7.52 (d, J = 1.8 Hz, 1H), 7.26 (d, J = 8.8 Hz, 2H), 6.72 (br s, 2H), 5.28 (s, 2H), 3.49 (m, 4H), 3.28 (t, 2H), 2.89 (t, 2H), 2.31 (m, 4H)	539
I-248		2-Piperidin-1-yl-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide	0.114	see examples	(300 MHz, $CDCl_3$) δ 7.93 (d, J = 1.8 Hz, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7.30 (m, 2H), 7.24 (m, 2H), 7.20 (m, 1H), 7.07 (m, 1H), 5.28 (s, 2H), 4.70 (br s, 2H), 3.28 (t, 2H), 2.82 (t, 2H), 2.62 (m, 4H), 1.85 (m, 4H), 1.63 (m, 2H)	537
I-249		2-Dimethylamino-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide	0.088	see examples	(300 MHz, $CDCl_3$) δ 7.92 (d, J = 1.8 Hz, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7.30 (m, 2H), 7.24 (m, 2H), 7.20 (m, 1H), 7.07 (m, 1H), 5.28 (s, 2H), 4.71 (br s, 2H), 3.20 (t, 2H), 2.88 (t, 2H), 2.32 (s, 6H)	497

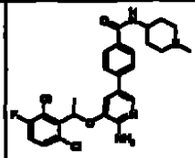
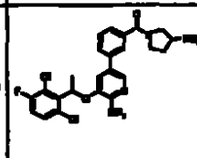
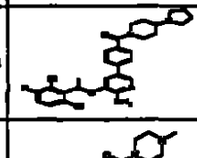
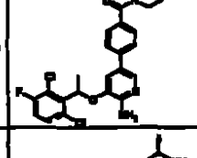
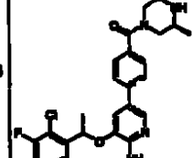
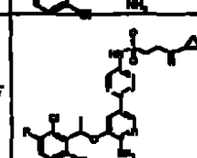
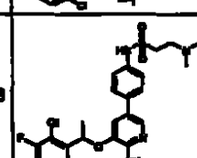
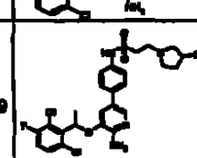
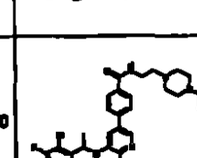
No.	Structure	Name	Mat IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-250		2-(4-Acetyl-piperazin-1-yl)-ethanesulfonic acid [4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl]-amide	0.42	see examples	(300 MHz, $CDCl_3$) δ 7.92 (d, J = 1.8 Hz, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7.30 (m, 2H), 7.24 (m, 1H), 7.20 (m, 1H), 7.07 (m, 2H), 5.28 (s, 2H), 4.80 (br s, 2H), 3.85 (m, 2H), 3.48 (m, 2H), 3.32 (t, 2H), 2.94 (t, 2H), 2.60 (m, 2H), 2.48 (m, 2H), 2.10 (s, 3H)	580
I-251		2-(Cyclopropylmethyl-amino)-ethanesulfonic acid [4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl]-amide	0.075	see examples	(300 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.49 (m, 2H), 7.31 (m, 3H), 7.21 (m, 1H), 7.16 (m, 1H), 5.28 (s, 2H), 4.76 (s, 2H), 3.23 (m, 4H), 2.56 (m, 2H), 1.00 (m, 1H), 0.59 (m, 2H), 0.18 (m, 2H)	523
I-252		2-[(3R)-3-Hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid [4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl]-amide	0.125	see examples	(300 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.48 (m, 2H), 7.31 (m, 3H), 7.19 (m, 1H), 7.05 (m, 1H), 5.28 (s, 2H), 4.75 (s, 2H), 4.45 (m, 1H), 3.29 (m, 2H), 3.10 (m, 3H), 2.88 (m, 1H), 2.61 (m, 1H), 2.30 (m, 2H), 1.89 (m, 2H)	539
I-253		2-[(2S)-2-Hydroxymethyl-pyrrolidin-1-yl]-ethanesulfonic acid [4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl]-amide	0.097	see examples	(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.48 (m, 2H), 7.30 (m, 3H), 7.21 (m, 1H), 7.06 (m, 1H), 5.31 (s, 2H), 4.75 (s, 2H), 3.55 (m, 2H), 3.36 (t, 1H), 3.11 (m, 2H), 2.89 (m, 2H), 2.21 (m, 1H), 1.88 (m, 6H)	553
I-254		2-[4-(2-Hydroxy-acetyl)-piperazin-1-yl]-ethanesulfonic acid [4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl]-amide	0.18	see examples	(300 MHz, DMSO-d_6) δ 9.81 (s, 1H), 7.89 (s, 1H), 7.58 (d, 2H), 7.50 (s, 1H), 7.39 (m, 2H), 7.24 (d, 2H), 6.75 (s, 2H), 5.28 (s, 2H), 4.84 (t, 1H), 4.01 (d, 2H), 3.29 (m, 6H), 2.79 (t, 2H), 2.38 (m, 4H)	596
I-255		2-(4-Acetyl-piperazin-1-yl)-ethanesulfonic acid [3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl]-amide	0.68	see examples	(300 MHz, $CDCl_3$) δ 2.02 (s, 3H), 2.30 (m, 4H), 2.99 (m, 4H), 3.35 (m, 4H), 3.56 (m, 2H), 5.30 (d, 2H), 5.42 (s, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.38 (m, 5H), 8.00 (d, 1H), 10.17 (s, 1H)	580
I-256		2-Pyrrolidin-1-yl-ethanesulfonic acid [3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl]-amide	0.23	see examples	(300 MHz, $CDCl_3$) δ 1.80-1.90 (m, 4H), 2.40-2.55 (m, 4H), 3.02 (t, J = 6.6 Hz, 2H), 3.29 (t, J = 6.6 Hz, 2H), 5.08 (s, 2H), 5.29 (d, J = 1.3 Hz, 2H), 6.95-7.05 (m, 1H), 7.10-7.20 (m, 1H), 7.25-7.45 (m, 6H), 7.97 (d, J = 1.7 Hz, 1 H)	524
I-257		2-Morpholin-4-yl-ethanesulfonic acid [3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl]-amide	1.64	see examples	(300 MHz, $CDCl_3$) δ 2.42 (t, J = 4.8 Hz, 4H), 2.90 (t, J = 6.9 Hz, 2H), 3.31 (t, J = 6.9 Hz, 2H), 3.82 (t, J = 4.8 Hz, 4H), 5.24 (s, 2H), 5.30 (d, J = 1.3 Hz, 2H), 6.95-7.05 (m, 1H), 7.10-7.20 (m, 1H), 7.30-7.45 (m, 6H), 7.99 (d, J = 1.8 Hz, 1H), 9.38 (s, 1H)	540
I-258		2-Diethylamino-ethanesulfonic acid [3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl]-amide	1.67	see examples	(300 MHz, $CDCl_3$) δ 1.00 (t, 6H), 2.52 (q, 4H), 3.02 (t, 2H), 3.28 (t, 2H), 5.19 (s, 2H), 5.29 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.36 (m, 5H), 7.99 (d, 1H)	526
I-259		2-Dimethylamino-ethanesulfonic acid [3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl]-amide	1.5	see examples	(300 MHz, $CDCl_3$) δ 2.24 (s, 6H), 2.85 (t, 2H), 3.24 (t, 2H), 5.11 (s, 2H), 5.29 (d, 2H), 7.07 (m, 1H), 7.15 (m, 1H), 7.35 (m, 5H), 7.98 (d, 1H)	498

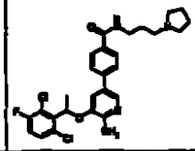
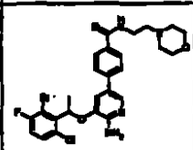
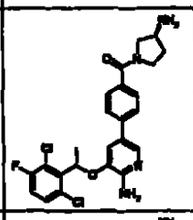
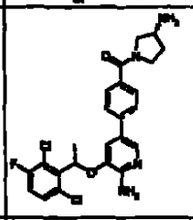
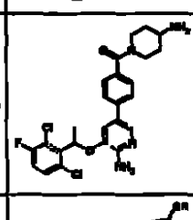
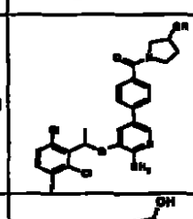
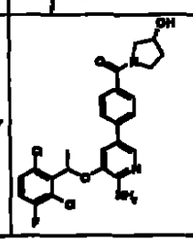
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-260		2-Piperidin-1-yl-ethanesulfonic acid [3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl]-amide	1.63	see examples	(300 MHz, $CDCl_3$) δ 1.30-1.80 (m, 6H), 2.30-2.45 (m, 4H), 2.89 (t, J = 6.7 Hz, 2H), 3.28 (t, J = 6.7 Hz, 2H), 5.13 (s, 2H), 5.29 (d, J = 1.4 Hz, 2H), 6.95-7.05 (m, 1H), 7.15-7.45 (m, 6H), 7.68 (d, J = 1.8 Hz, 1H)	538
I-261		2-[(3R)-3-Hydroxymethyl-pyrrolidin-1-yl]-ethanesulfonic acid [3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl]-amide	1.7	see examples	(300 MHz, $CDCl_3$) δ 1.60-1.8 (m, 4H), 2.05-2.15 (m, 1H), 2.55-2.75 (m, 2H), 2.95-3.15 (m, 2H), 3.25-3.55 (m, 3H), 3.82 (dd, J = 3.0, 11.2 Hz, 1H), 4.97 (s, 2H), 5.28 (d, J = 1.8 Hz, 2H), 6.95-7.05 (m, 1H), 7.10-7.20 (m, 1H), 7.25-7.45 (m, 5H), 7.66 (d, J=1.8 Hz, 1H)	554
I-262		2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid [3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl]-amide	1.5	see examples	(300 MHz, DMSO-d_6) δ 1.15-1.30 (m, 2H), 1.45-1.65 (m, 2H), 1.80-2.02 (m, 2H), 2.60-2.70 (m, 4H), 4.49 (bra, 1H), 5.28 (s, 2H), 5.82 (s, 2H), 7.05-7.10 (m, 1H), 7.20-7.40 (m, 6H), 7.45-7.60 (m, 1H), 7.83 (d, J = 1.8 Hz, 1H)	554
I-263		2-[4-(2-Hydroxy-acetyl)-piperazin-1-yl]-ethanesulfonic acid [3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl]-amide	1.14	see examples	(300 MHz, $CDCl_3$) δ 2.36 (m, 4H), 2.62 (t, 2H), 3.14 (m, 2H), 3.32 (t, 2H), 3.64 (m, 2H), 3.80 (br s, 1H), 4.07 (s, 2H), 5.30 (s, 2H), 5.40 (br s, 2H), 7.06 (m, 1H), 7.24 (m, 2H), 7.34(m, 2H), 7.44 (m, 2H), 7.99 (d, J = 1.8 Hz, 1H), 8.68 (br s, 1H)	598
I-264		2-[(3R)-3-Hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid [3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl]-amide	1.097	see examples	(300 MHz, $CDCl_3$) δ 1.65 (m, 1H), 2.06 (m, 1H), 2.22 (m, 1H), 2.46 (m, 1H), 2.76 (m, 1H), 2.87 (m, 1H), 3.02 (m, 2H), 3.32 (m, 2H), 4.28 (m, 1H), 5.28 (br s, 2H), 5.29 (s, 2H), 7.06 (m, 1H), 7.24 (m, 2H), 7.44(m, 6H), 8.00 (d, J = 1.7 Hz, 1H)	539
I-265		2-(Cyclopropylmethyl-amino)-ethanesulfonic acid [3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl]-amide	1	see examples	(300 MHz, $CDCl_3$) δ 0.02 (m, 2H), 0.39 (m, 2H), 0.84 (m, 1H), 2.40 (d, 2H), 3.14 (t, 2H), 3.32 (t, 2H), 5.28 (s, 2H), 5.38 (br s, 2H), 7.06 (m, 1H), 7.24 (m, 2H), 7.44(m, 6H), 8.00 (d, J = 1.7 Hz, 1H)	523
I-266		2-Cyclopropylamino-ethanesulfonic acid [3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl]-amide	0.9	see examples	(300 MHz, $CDCl_3$) δ 0.28 (m, 2H), 0.37 (m, 2H), 2.09 (m, 1H), 3.15-3.40 (m, 4H), 5.30 (d, 2H), 5.39 (s, 2H), 7.07 (m, 1H), 7.19 (m, 1H), 7.30-7.55 (m, 6H), 8.01 (d, 1H)	509
I-267		3-(2-Chloro-3,6-difluoro-benzyloxy)-5-(2-dimethylaminomethyl-phenyl)-pyridin-2-ylamine; compound with trifluoro-acetic acid		see examples	-	404
I-268		3-(2-Chloro-3,6-difluoro-benzyloxy)-5-(3-pyrrolidin-1-yl-phenyl)-pyridin-2-ylamine; compound with trifluoro-acetic acid	4	see examples	(400 MHz, DMSO-d_6) δ 1.94 (t, 4H), 3.31 (t, 4H), 5.44 (s, 2H), 6.56 (d, 1H), 6.74 (s, 1H), 6.88 (d, 1H), 7.24 (t, 1H), 7.43 (m, 1H), 7.66 (m, 3H), 7.83 (m, 2H)	416

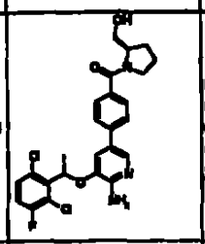
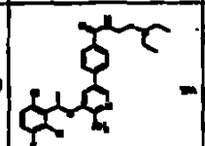
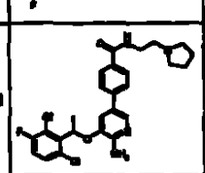
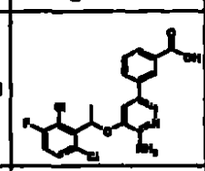
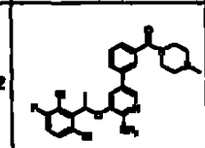
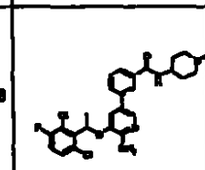
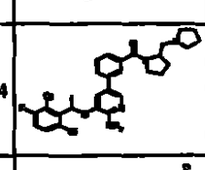
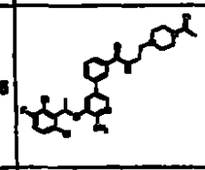
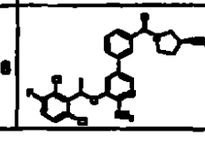
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-269		*N*-{4-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-methanesulfonamide; compound with trifluoro-acetic acid		see examples	(400 MHz, DMSO-d_6) δ 2.99 (s, 3H), 6.35 (s, 2H), 6.72 (br s, 2H), 7.27 (d, 2H), 7.42 (m, 1H), 7.69 (m, 1H), 7.85 (d, 2H), 7.73 (s, 1H), 7.84 (s, 1H), 9.79 (s, 1H)	440
I-270		5-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophene-2-carboxylic acid		see examples		397
I-271		{5-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophen-2-yl}-(4-methyl-piperazin-1-yl)-methanone		see examples	(300 MHz, $CDCl_3$) δ 8.00 (d, *J* = 1.8 Hz, 1H), 7.30 (d, *J* = 1.8 Hz, 1H), 7.25 (d, *J* = 1.5 Hz, 1H), 7.20 (m, 1H), 7.10 (d, *J* = 3.8 Hz, 1H), 7.07 (m, 1H), 5.27 (d, *J* = 1.7 Hz, 2H), 4.82 (br s, 2H), 3.81 (m, 4H), 2.47 (m, 4H), 2.34 (s, 3H)	479
I-272		{5-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophen-2-yl}-[(2R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone		see examples	(300 MHz, $CDCl_3$) δ 8.02 (d, *J* = 1.8 Hz, 1H), 7.82 (m, 1H), 7.32 (d, *J* = 1.8 Hz, 1H), 7.21 (m, 1H), 7.14 (d, *J* = 3.9 Hz, 1H), 7.07 (m, 1H), 5.27 (d, *J* = 1.5 Hz, 2H), 4.80 (br s, 2H), 4.50 (m, 1H), 3.81 (m, 3H), 2.74 (m, 4H), 2.25-1.82 (m, 10H).	533
I-273		5-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophene-2-carboxylic acid (1-methyl-piperidin-4-yl)-amide		see examples	(300 MHz, $CDCl_3$) δ 8.02 (d, *J* = 1.8 Hz, 1H), 7.42 (d, *J* = 3.8 Hz, 1H), 7.29 (d, *J* = 1.8 Hz, 1H), 7.21 (m, 1H), 7.15 (d, *J* = 3.9 Hz, 1H), 7.07 (m, 1H), 6.69 (br d, 1H), 5.28 (d, *J* = 1.8 Hz, 2H), 4.82 (br s, 2H), 4.05 (m, 1H), 3.06 (m, 2H), 2.60 (s, 3H), 2.40 (m, 2H), 1.90 (m, 2H), 1.62 (m, 2H)	493
I-274		{5-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophen-2-yl}-(3,5-dimethyl-piperazin-1-yl)-methanone		see examples	(300 MHz, $CDCl_3$) δ 8.00 (d, *J* = 1.8 Hz, 1H), 7.30 (d, *J* = 1.8 Hz, 1H), 7.24 (d, *J* = 3.8 Hz, 1H), 7.21 (m, 1H), 7.10 (d, *J* = 3.8 Hz, 1H), 7.07 (m, 1H), 5.28 (d, *J* = 1.5 Hz, 2H), 4.82 (br s, 2H), 4.38 (m, 2H), 2.88 (m, 2H), 2.85 (m, 2H), 1.58 (br s, 1H), 1.11 (d, *J* = 6.2 Hz, 6H)	493
I-275		5-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophene-2-carboxylic acid (2-pyrrolidin-1-yl-ethyl)-amide		see examples	(300 MHz, $CDCl_3$) δ 8.00 (d, *J* = 1.8 Hz, 1H), 7.82 (br m, 1H), 7.66 (d, *J* = 3.9 Hz, 1H), 7.29 (d, *J* = 1.8 Hz, 1H), 7.21 (m, 1H), 7.11 (d, *J* = 3.8 Hz, 1H), 7.07 (m, 1H), 5.28 (d, *J* = 1.5 Hz, 2H), 4.81 (br s, 2H), 3.71 (m, 2H), 3.02 (m, 2H), 2.95 (m, 2H), 2.01 (m, 4H), 1.97 (m, 2H), 1.11 (d, *J* = 6.2 Hz, 6H)	493
I-276		{5-[6-Amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophen-2-yl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone		see examples	(300 MHz, $CDCl_3$) δ 8.00 (d, *J* = 1.8 Hz, 1H), 7.29 (d, *J* = 1.8 Hz, 1H), 7.24 (d, *J* = 3.8 Hz, 1H), 7.20 (m, 1H), 7.09 (d, *J* = 3.8 Hz, 1H), 7.07 (m, 1H), 5.27 (d, *J* = 1.5 Hz, 2H), 4.80 (br s, 2H), 4.43 (m, 2H), 3.10 (m, 2H), 2.63 (m, 4H), 2.34 (m, 1H), 1.98 (m, 2H), 1.83 (m, 4H), 1.63 (m, 2H).	533

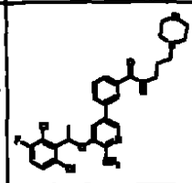
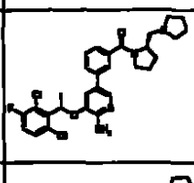
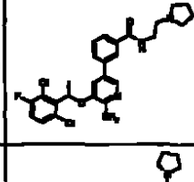
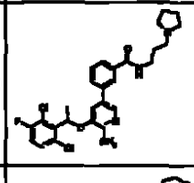
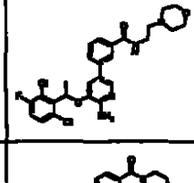
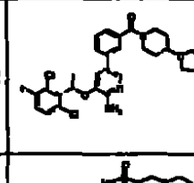
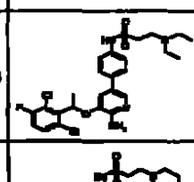
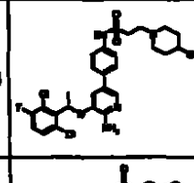
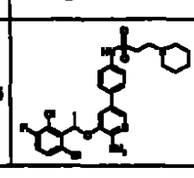
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-277		4-[6-Amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-benzoic acid		see examples		407
I-278		[4-[6-Amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl]-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone		see examples	(300 MHz, $CDCl_3$) δ 7.97 (d, J = 1.8 Hz, 1H), 7.81-7.42 (m, 6H), 7.21 (d, J = 8.7 Hz, 1H), 7.12 (d, J = 1.8 Hz, 1H), 5.33 (s, 2H), 4.81 (br s, 2H), 4.62 (m, 1H), 3.84 (m, 1H), 2.99 (m, 2H), 2.85 (m, 4H), 2.32 (m, 1H), 1.97 (m, 2H), 1.84 (m, 4H), 1.60 (m, 2H)	543
I-279		4-[6-Amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-N-(1-methyl-piperidin-4-yl)-benzamide		see examples	(300 MHz, $CDCl_3$) δ 7.99 (d, J = 1.8 Hz, 1H), 7.80 (d, J = 8.3 Hz, 2H), 7.65 (m, 1H), 7.62 (d, J = 8.3 Hz, 2H), 7.44 (d, J = 7.8 Hz, 1H), 7.22 (t, J = 8.7 Hz, 1H), 7.12 (d, J = 1.8 Hz, 1H), 5.99 (br d, 1H), 5.34 (s, 2H), 4.83 (br s, 2H), 4.04 (m, 1H), 2.87 (m, 2H), 2.34 (s, 3H), 2.20 (m, 2H), 2.06 (m, 2H), 1.83 (m, 2H)	503
I-280		[4-[6-Amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl]-(3,5-dimethyl-piperazin-1-yl)-methanone		see examples	(300 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.81-7.43 (m, 6H), 7.22 (t, J = 8.7 Hz, 1H), 7.13 (d, J = 1.5 Hz, 1H), 5.33 (s, 2H), 4.82 (br s, 2H), 4.65 (m, 1H), 3.85 (m, 1H), 2.90 (m, 2H), 2.68 (m, 1H), 2.42 (m, 1H), 1.80 (m, 1H), 1.12 (d, 3H), 1.00 (d, 3H)	503
I-281		[4-[6-Amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl]-(3-dimethylamino-pyrrolidin-1-yl)-methanone		see examples	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 2.4 Hz, 1H), 7.81-7.43 (m, 6H), 7.21 (t, J = 8.8 Hz, 1H), 7.14 (d, J = 2.4 Hz, 1H), 5.33 (s, 2H), 4.87 (br s, 2H), 3.89 (m, 1H), 3.66 (m, 2H), 3.42 (m, 1H), 2.70 (m, 1H), 2.32 (s, 3H), 2.23 (s, 3H), 2.14 (m, 1H), 1.62 (m, 1H)	503
I-282		[4-[6-Amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl]-[(2S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone		see examples	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.4 Hz, 1H), 7.58-7.43 (m, 6H), 7.20 (t, J = 8.8 Hz, 1H), 7.13 (d, J = 1.4 Hz, 1H), 5.34 (s, 2H), 4.81 (br s, 2H), 4.48 (m, 1H), 3.60 (m, 2H), 2.77 (m, 4H), 2.30-1.50 (m, 10H)	543
I-283		4-[6-Amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-6N-(2-morpholin-4-yl-ethyl)-benzamide		see examples	(300 MHz, $CDCl_3$) δ 8.00 (d, J = 1.2 Hz, 1H), 7.83 (d, J = 8.2 Hz, 2H), 7.58 (m, 1H), 7.55 (d, J = 8.2 Hz, 2H), 7.45 (d, 1H), 7.20 (t, J = 8.8 Hz, 1H), 7.13 (d, J = 1.4 Hz, 1H), 6.79 (m, 1H), 5.34 (s, 2H), 4.85 (br s, 2H), 3.74 (m, 4H), 3.55 (m, 2H), 2.62 (m, 2H), 2.52 (m, 4H)	519

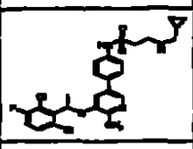
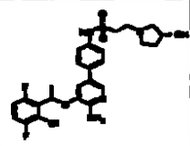
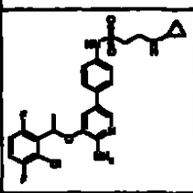
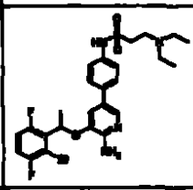
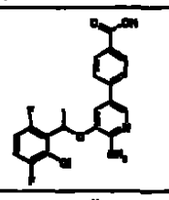
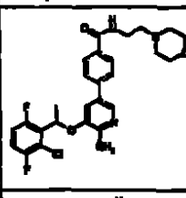
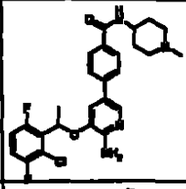
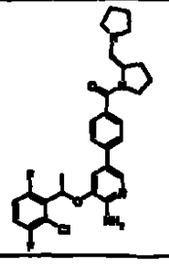
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-284		(4-[6-Amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone		see examples	(300 MHz, $CDCl_3$) δ 7.97 (d, J = 1.8 Hz, 1H), 7.58-7.43 (m, 6H), 7.20 (t, J = 8.8 Hz, 1H), 7.12 (d, J = 1.8 Hz, 1H), 5.34 (s, 2H), 4.83 (br s, 2H), 3.80 (m, 2H), 3.66 (m, 2H), 2.44 (m, 4H), 2.33 (s, 3H)	499
I-285		*N*-[2-(4-Acetyl-piperazin-1-yl)-ethyl]-4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-benzamide		see examples	(300 MHz, $CDCl_3$) δ 8.00 (d, J = 1.2 Hz, 1H), 7.82 (d, J = 8.2 Hz, 2H), 7.58 (m, 1H), 7.55 (d, J = 8.2 Hz, 2H), 7.44 (d, J = 7.8 Hz, 1H), 7.22 (t, J = 8.8 Hz, 1H), 7.14 (d, J = 1.4 Hz, 1H), 6.72 (m, 1H), 5.34 (s, 2H), 4.85 (br s, 2H), 3.85 (m, 2H), 3.60 (m, 2H), 3.50 (m, 2H), 2.65 (m, 2H), 2.51 (m, 4H), 2.10 (s, 3H)	660
I-286		2-Piperidin-1-yl-ethanesulfonic acid (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.18	see examples	(300MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.28 (d, 2H), 7.20 (d, 2H), 7.06 (m, 3H), 7.59 (s, 1H), 4.88 (s, 2H), 3.25 (m, 2H), 2.89 (m, 2H), 2.49 (m, 4H), 1.83 (d, 3H), 1.62 (m, 4H), 1.48 (m, 2H)	551
I-287		2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.14	see examples	(300MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.28 (d, 2H), 7.20 (d, 2H), 7.06 (m, 3H), 7.59 (s, 1H), 4.88 (s, 2H), 3.78 (m, 1H), 3.25 (m, 2H), 2.89 (m, 2H), 2.78 (m, 2H), 2.28 (m, 2H), 1.83 (m, 5H), 1.62 (m, 2H)	567
I-288		2-Dimethylamino-ethanesulfonic acid (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.15	see examples	(300MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.28 (d, 2H), 7.20 (d, 2H), 7.06 (m, 3H), 7.59 (s, 1H), 4.88 (s, 2H), 3.21 (m, 2H), 2.88 (m, 2H), 2.30 (s, 6H), 2.28 (m, 2H), 1.82 (d, 3H)	511
I-289		2-Cyclopropylamino-ethanesulfonic acid (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.16	see examples	(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.56 (d, 2H), 7.52 (d, 2H), 7.16 (m, 3H), 6.85 (m, 1H), 4.89 (s, 2H), 3.22 (m, 4H), 2.14 (m, 1H), 1.85 (d, 3H), 0.60 (m, 2H), 0.38 (m, 2H)	523
I-290		4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid		see examples		422
I-291		(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-[(2R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.063	see examples	(300MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.52 (d, 2H), 7.31 (d, 2H), 7.06 (m, 3H), 6.13 (m, 1H), 4.86 (s, 2H), 4.30 (m, 1H), 3.40 (m, 2H), 2.60 (m, 4H), 1.82 (d, 3H), 1.70-2.0 (m, 10H)	657

No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-292		4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(1-methyl-piperidin-4-yl)-benzamide	0.089	see examples	(300MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.76 (d, 2H), 7.35 (d, 2H), 7.31 (m, 3H), 6.16 (bart, 1H), 5.90 (d, 1H), 4.88 (s, 2H), 4.05 (m, 1H), 2.85 (d, 1H), 2.38 (s, 3H), 2.08 (d, 1H), 2.25 (t, 1H), 1.82 (d, 3H), 1.80 (m, 1H), 1.29(m, 2H), 0.88(m, 2H)	559
I-293		(3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-[(3R)-3-amino-pyrrolidin-1-yl]-methanone	0.051	see examples	(300MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.81 (s, 1H), 7.38 (m, 3H), 7.30 (m, 1H), 7.16 (m, 1H), 6.87 (s, 1H), 6.15 (m, 1H), 4.84(s, 2H), 3.45-3.89 (m, 4H), 3.20(m, 1H), 2.25(m, 1H), 2.15 (m, 1H), 1.82 (d, 3H), 1.34 (m, 2H)	489
I-294		(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.082	see examples	(300MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.70 (m, 1H), 7.45 (m, 1H), 7.30 (s, 2H), 7.08 (t, 1H), 6.82 (d, 2H), 6.13 (m, 1H), 4.86 (s, 2H), 4.30 (t, 1H), 2.80 (m, 4H), 1.82 (d, 3H), 1.80 (m, 4H), 1.35 (m, 4H), 0.89 (m, 4H)	559
I-295		(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone	0.078	see examples	(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.71 (d, 2H), 7.49 (d, 2H), 7.40 (s, 1H), 7.35 (m, 1H), 7.09 (m, 1H), 6.17 (m, 1H), 4.98 (s, 2H), 4.28 (t, 2H), 3.85 (m, 4H), 2.38 (m, 2H), 2.31 (s, 3H), 1.88 (d, 3H)	503
I-296		(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(3,5-dimethyl-piperazin-1-yl)-methanone	0.054	see examples		
I-297		2-Cyclopropylamino-ethanesulfonic acid (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.184	see example:	(300 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.30 (m, 3H), 7.24 (m, 3H), 7.08 (t, 1H), 6.95 (c, 1H), 6.09 (m, 1H), 4.89 (c, 2H), 3.21 (m, 3H), 2.12 (m, 1H), 1.84 (d, 3H), 0.87 (m, 1H), 0.50 (m, 2H), 0.29 (m, 2H)	539
I-298		2-Dimethylamino-ethanesulfonic acid (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.059	see examples	(300 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.28 (m, 6H), 7.04 (t, 1H), 6.84 (s, 1H), 6.12 (m, 1H), 4.93 (s, 2H), 3.21 (t, 2H), 2.85 (t, 2H), 2.31 (s, 6H), 1.85 (d, 3H)	527
I-299		2-[(3R)-3-Hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.082	see examples	(300MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.30 (m, 6H), 7.10 (t, 1H), 6.89 (s, 1H), 6.10 (bart, 1H), 4.86 (s, 2H), 4.40 (s, 1H), 3.21 (m, 2H), 2.88 (m, 3H), 2.67 (d, 1H), 2.48 (m, 1H), 2.20 (m, 2H), 2.05 (s, 1H), 1.86 (d, 3H), 1.25 (s, 1H)	570
I-300		N-[2-(4-Acetyl-piperazin-1-yl)-ethyl]-4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzamide	0.059	4 as in Example I-291	(300MHZ, CDCl3) δ 7.85 (s, 1H), 7.79 (d, 2H), 7.42 (d, 2H), 7.30 (dd, 1H), 7.07 (t, 1H), 7.02 (d, 1H), 6.81 (bm, 1H), 6.13 (q, 1H), 5.42 (s, 2H), 3.80 (m, 2H), 3.62 (m, 2H), 3.53 (m, 2H), 2.68 (m, 2H), 2.62 (m, 4H), 2.10 (s, 3H), 1.87 (d, 3H).	575 [M+1]

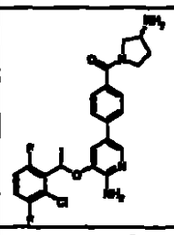
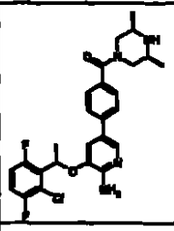
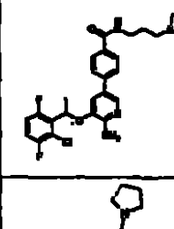
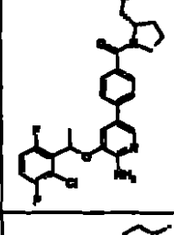
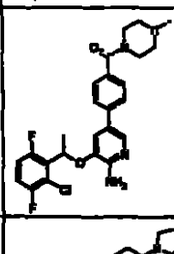
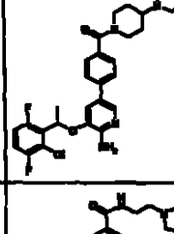
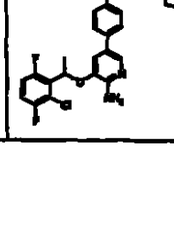
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-301		4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide	0.084	4 as in Example I-291	(300MHZ, CDCl3) δ 8.71 (bm, 1H), 7.92 (m, 3H), 7.42 (d, 2H), 7.31 (dd, 1H), 7.08 (t, 1H), 7.01 (s, 1H), 6.12 (q, 1H), 4.97 (s, 2H), 3.65 (m, 2H), 3.00 (m, 6H), 2.00 (m, 6H), 1.87 (d, 3H).	533 [M+1]
I-302		4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide	0.071	4 as in Example I-291)	(300MHZ, CDCl3) δ 7.90 (d, 1H), 7.79 (d, 2H), 7.44 (d, 2H), 7.31 (dd, 1H), 7.08 (t, 1H), 7.01 (d, 1H), 6.83 (bm, 1H), 6.12 (q, 1H), 5.05 (s, 2H), 3.74 (m, 4H), 3.68 (m, 2H), 2.63 (m, 2H), 2.63 (m, 4H), 1.87 (d, 3H).	533 [M+1]
I-303		(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone	0.058	4 as in Example I-291	(300MHZ, CD3OD) δ 7.76 (s, 1H),7.54 (m, 1H), 7.42 (m, 4H), 7.24 (t, 1H), 7.04 (s, 1H), 6.22 (q, 1H), 4.82 (s, 2H), 3.76 (m, 1H), 3.68 (m, 2H), 3.52 (m, 1H), 2.28 (m, 1H), 1.82 (m, 3H), 1.76 (m, 1H), 1.42 (m, 1H).	491 [M+1]
I-304		(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone	0.072	4 as in Example I-291	(300MHZ, CD3OD) δ 7.76 (s, 1H),7.54 (m, 1H), 7.42 (m, 4H), 7.24 (t, 1H), 7.04 (s, 1H), 6.22 (q, 1H), 4.82 (s, 2H), 3.76 (m, 1H), 3.68 (m, 2H), 3.52 (m, 1H), 2.28 (m, 1H), 1.82 (m, 3H), 1.76 (m, 1H), 1.42 (m, 1H).	491 [M+1]
I-305		(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-amino-piperidin-1-yl)-methanone	0.18	4 as in Example I-291		504 [M+1]
I-306		(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-3-hydroxy-pyrrolidin-1-yl)-methanone	0.024	4 as in Example I-291	(300MHZ, CD3OD) δ 7.76 (d, 1H), 7.47 (m, 3H), 7.37 (m, 3H), 6.92 (d, 1H), 6.07 (q, 1H), 5.89 (s, 2H), 4.82 (dd, 1H), 4.15 (d, 1H), 3.53 (m, 2H), 3.42 (m, 1H), 3.15 (m, 1H), 2.43 (m, 1H), 1.85 (m, 1H), 1.76 (d, 3H).	491 [M+1]
I-307		(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-3-hydroxy-pyrrolidin-1-yl)-methanone	0.022	4 as in Example I-291	(300MHZ, CD3OD) δ 7.80 (d, 1H), 7.47 (m, 3H), 7.37 (m, 3H), 6.92 (d, 1H), 6.07 (q, 1H), 5.89 (s, 2H), 4.82 (dd, 1H), 4.15 (d, 1H), 3.83 (m, 2H), 3.42 (m, 1H), 3.15 (m, 1H), 2.43 (m, 1H), 1.85 (m, 1H), 1.76 (d, 3H).	491 [M+1]

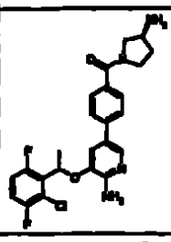
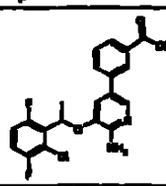
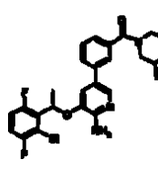
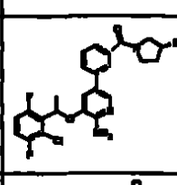
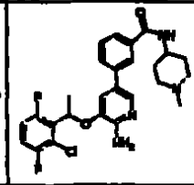
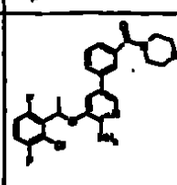
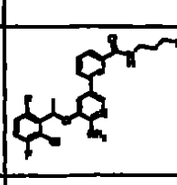
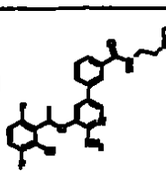
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-308		(4-{6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((R)-2-hydroxymethyl-pyrrolidin-1-yl)-methanone	0.033	4 as in Example I-291	(300MHZ, CD3OD) δ 7.80 (d, 1H), 7.47 (m, 3H), 7.37 (m, 3H), 6.92 (d, 1H), 6.07 (q, 1H), 5.89 (s, 2H), 4.70 (m, 1H), 4.05 (m, 1H), 3.6 (m, 2H), 3.32 (m, 1H), 2.43 (m, 1H), 1.85 (m, 3H), 1.78 (d, 3H), 1.15(m, 1H).	505 [M+1]
I-309		4-{6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-diethylamino-ethyl)-benzamide	0.04	4 as in Example I-291	(300MHZ, CDCl3) δ 8.53 (bm, 1H), 8.00 (t, 1H), 7.95 (s, 1H), 7.68 (d, 2H), 7.56 (m, 3H), 7.45 (t, 1H), 7.09 (d, 1H), 6.23 (q, 1H), 3.60 (q, 2H), 3.22 (m, 6H), 3.09 (m, 1H), 1.85 (d, 3H), 1.22 (dd, 6H).	519 [M+1]
I-310		4-{6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide	0.12	4 as in Example I-291	(300MHZ, CDCl3) δ 8.25 (bm, 1H), 7.90 (d, 1H), 7.82 (s, 2H), 7.34 (d, 2H), 7.29 (m, 1H), 7.04 (t, 1H), 6.98 (s, 1H), 6.09 (q, 1H), 4.87 (s, 2H), 3.82 (m, 2H), 3.18 (m, 6H), 2.00 (m, 4H), 1.85 (d, 3H).	518 [M+1]
I-311		3-{6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-benzoic acid		3 as in Example 211		420 [M-1]
I-312		(3-{6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone	0.052	4	(300MHZ, CDCl3) δ 7.86 (s, 1H), 7.41 (m, 3H), 7.30 (m, 3H), 7.07 (t, 1H), 6.99 (s, 1H), 6.12 (q, 1H), 4.99 (s, 2H), 3.86 (m, 2H), 3.50 (m, 2H), 2.64 (m, 2H), 2.40 (m, 2H), 2.36 (s, 3H), 1.87 (d, 3H).	503 [M+1]
I-313		3-{6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(1-methyl-piperidin-4-yl)-benzamide	0.059	4 as in Example I-312	(300MHZ, CDCl3) δ 7.89 (t, 1H), 7.76 (s, 1H), 7.67 (d, 1H), 7.48 (d, 1H), 7.42 (t, 1H), 7.31 (dd, 1H), 7.05 (t, 1H), 7.01 (s, 1H), 6.29 (bd, 1H), 6.12 (q, 1H), 4.99 (s, 2H), 4.08 (m, 1H), 3.04 (m, 2H), 2.42 (s, 3H), 2.32 (m, 2H), 2.10 (m, 2H), 1.87 (d, 3H), 1.80 (m, 2H).	517 [M+1]
I-314		(3-{6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.06	4 as in Example I-312	(300MHZ, CDCl3) δ 7.87 (s, 1H), 7.40 (m, 4H), 7.29 (dd, 1H), 7.05 (t, 1H), 7.00 (s, 1H), 6.12 (q, 1H), 4.92 (s, 2H), 3.50 (m, 2H), 3.74 (m, 4H), 1.89 (d, 3H), 1.67-2.18 (m, 11H).	559 [M+1]
I-315		N-[2-(4-Acetyl-piperazin-1-yl)-ethyl]-3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-benzamide	0.069	4 as in Example I-312	(300MHZ, CDCl3) δ 7.88 (s, 1H), 7.83 (s, 1H), 7.65 (d, 1H), 7.48 (m, 2H), 7.32 (dd, 1H), 7.06 (t, 1H), 7.03 (s, 1H), 6.95 (bt, 1H), 6.12 (q, 1H), 5.08 (s, 2H), 3.69 (m, 4H), 3.60 (m, 2H), 2.73 (m, 2H), 2.52 (m, 4H), 2.09 (s, 3H), 1.87 (d, 3H).	576 [M+1]
I-316		(3-{6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone	0.048	4 as in Example I-312	(300MHZ, CDCl3) δ 7.87 (s, 1H), 7.38 (m, 4H), 7.29 (m, 1H), 7.06 (t, 1H), 6.96 (s, 1H), 6.12 (q, 1H), 5.05 (s, 2H), 3.82 (m, 2H), 3.72 (m, 2H), 2.10 (m, 1H), 1.86 (d, 3H), 1.84 (m, 2H).	491 [M+1]

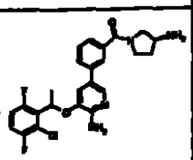
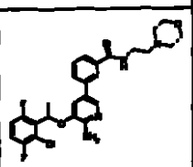
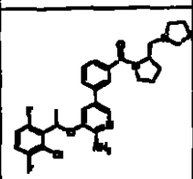
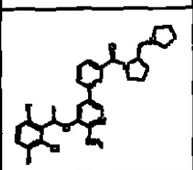
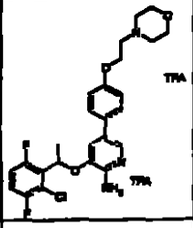
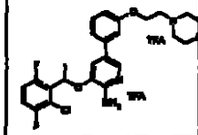
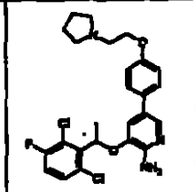
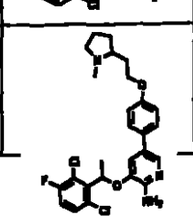
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-317		3-[5-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(3-morpholin-4-yl-propyl)-benzamide	0.059	4 as in Example I-312	(300MHZ, CDCl3) δ 7.91 (s, 1H), 7.87 (s, 1H), 7.85 (d, 1H), 7.50 (m, 2H), 7.31 (dd, 1H), 7.04(m, 2H), 6.13 (q, 1H), 4.93 (s, 2H), 3.84 (m, 6H), 2.80 (m, 6H), 1.87 (d, 3H), 1.81 (m, 2H).	549 [M+1]
I-318		(3-[5-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.13	4 as in Example I-312	(300MHZ, CDCl3) δ 7.87 (s, 1H), 7.40 (m, 4H), 7.29 (dd, 1H), 7.05 (t, 1H), 7.00 (s, 1H), 6.12 (q, 1H), 4.92 (s, 2H), 3.50 (m, 2H), 3.74 (m, 4H), 1.86 (d, 3H), 1.57-2.15 (m, 11H).	556 [M+1]
I-319		3-[5-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide	0.1	4 as in Example I-312	(300MHZ, CDCl3) δ 7.89 (s, 1H), 7.82 (s, 1H), 7.73 (d, 1H), 7.48 (m, 4H), 7.22 (t, 1H), 7.04 (s, 1H), 6.95 (bt, 1H), 6.22 (q, 1H), 4.82 (s, 2H), 3.80 (m, 2H), 2.82 (m, 2H), 2.70 (m, 4H), 1.87 (d, 3H), 1.82 (m, 2H).	518 [M+1]
I-320		3-[5-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide	0.13	4 as in Example I-312	(300MHZ, CDCl3) δ 8.66 (bt, 1H), 7.90 (s, 1H), 7.85 (s, 1H), 7.81 (d, 1H), 7.42 (m, 2H), 7.31 (dd, 1H), 7.05 (m, 2H), 6.14 (q, 1H), 4.88 (s, 2H), 3.65 (m, 2H), 2.71 (m, 2H), 2.59 (m, 4H), 1.87 (d, 3H), 1.80 (m, 2H), 1.71 (m, 4H).	531 [M+1]
I-321		3-[5-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide	0.16	4 as in Example I-312	(300MHZ, CDCl3) δ 7.90 (s, 1H), 7.84 (s, 1H), 7.66 (d, 1H), 7.48 (m, 2H), 7.32 (dd, 1H), 7.05 (m, 2H), 6.66 (bt, 1H), 6.14 (q, 1H), 5.04 (s, 2H), 3.82 (m, 4H), 3.66 (m, 2H), 2.72 (t, 2H), 2.60 (m, 4H), 1.88 (d, 3H).	535 [M+1]
I-322		(3-[5-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(1-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.071	4 as in Example I-312	(300MHZ, CDCl3) δ 7.86 (s, 1H), 7.41 (m, 3H), 7.30 (m, 3H), 7.07 (t, 1H), 6.99 (s, 1H), 6.12 (q, 1H), 4.96 (s, 2H), 4.70 (m, 1H), 3.82 (m, 1H), 3.05 (m, 1H), 2.96 (m, 1H), 2.65 (m, 4H), 2.38 (m, 1H), 1.82 (m, 1H), 1.81 (m, 5H), 1.55 (m, 2H).	559 [M+1]
I-323		2-Diethylamino-ethanesulfonic acid (4-[5-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.08	9	(300MHZ, CDCl3) δ 7.83 (s, 1H), 7.32 (m, 4H), 7.21 (d, 2H), 7.06 (t, 1H), 6.98 (s, 1H), 5.98 (q, 1H), 4.81 (s, 2H), 3.22 (m, 2H), 3.02 (m, 2H), 2.62 (m, 4H), 1.84 (d, 3H), 1.08 (t, 6H).	571 [M+1]
I-324		2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid (4-[5-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.059	8 as in Example I-297	(300MHZ, CDCl3) δ 7.81 (s, 1H), 7.31 (m, 3H), 7.25 (m, 3H), 7.07 (t, 1H), 6.98 (s, 1H), 6.11 (q, 1H), 4.95 (s, 2H), 3.76 (m, 1H), 3.25 (t, 2H), 2.92 (t, 2H), 2.79 (m, 2H), 2.25 (m, 2H), 1.93 (m, 2H), 1.86 (d, 3H), 1.62 (m, 2H).	563 [M+1]
I-325		2-Piperidin-1-yl-ethanesulfonic acid (4-[5-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.059	9 as in Example I-297	(300MHZ, CDCl3) δ 7.84 (s, 1H), 7.32 (m, 4H), 7.21 (d, 2H), 7.06 (dd, 1H), 6.98 (s, 1H), 6.11 (q, 1H), 4.86 (s, 2H), 3.24 (t, 2H), 2.89 (t, 2H), 2.48 (m, 4H), 1.86 (d, 3H), 1.62 (m, 4H), 1.49 (m, 2H).	559 [M+1]

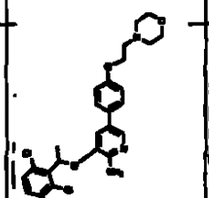
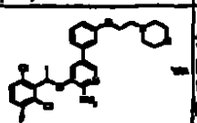
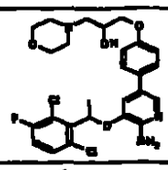
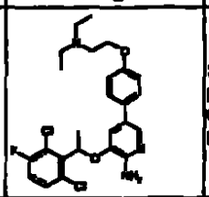
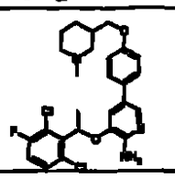
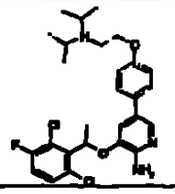
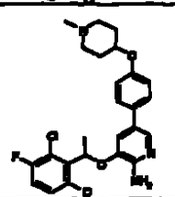
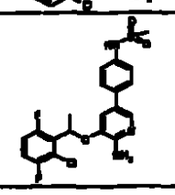
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-325		2-(Cyclopropylmethyl-amino)-ethanesulfonic acid (4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.075	9 as in Example I-287	(300MHZ, CDCl3) δ 7.83 (s, 1H), 7.28 (m, 6H), 7.06 (dd, 1H), 6.86 (s, 1H), 6.11 (q, 1H), 4.91 (s, 2H), 3.22 (m, 4H), 2.80 (d, 2H), 1.88 (d, 3H), 0.84 (m, 2H), 0.62 (m, 2H), 0.15 (m, 1H).	617 [M+1]
I-327		2-((R)-3-Hydroxy-pyrrolidin-1-yl)-ethanesulfonic acid (4-[5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.093	9 as in Example I-286	(300MHZ, CDCl3) δ 7.83 (s, 1H), 7.32 (m, 5H), 7.05 (m, 3H), 5.95 (q, 1H), 4.84 (s, 2H), 4.43 (m, 1H), 3.28 (m, 2H), 3.02 (m, 3H), 2.84 (m, 1H), 2.63 (m, 1H), 2.30 (m, 1H), 2.22 (m, 1H), 1.84 (d, 3H), 1.81 (m, 1H).	653 [M+1]
I-328		2-Cyclopropylamino-ethanesulfonic acid (4-[5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.16	9 as in Example I-286	(300MHZ, CDCl3) δ 7.89 (s, 1H), 7.38 (d, 2H), 7.24 (m, 2H), 7.18 (m, 3H), 5.86 (q, 1H), 4.89 (s, 2H), 3.22 (m, 4H), 2.14 (m, 1H), 1.85 (d, 3H), 0.60 (m, 2H), 0.36 (m, 2H).	623 [M+1]
I-329		2-Diethylamino-ethanesulfonic acid (4-[5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.095	9 as in Example I-286	(300MHZ, CDCl3) δ 7.84 (s, 1H), 7.34 (d, 2H), 7.23 (m, 3H), 7.02 (m, 3H), 5.86 (q, 1H), 4.81 (s, 2H), 3.22 (m, 2H), 3.02 (m, 2H), 2.82 (m, 4H), 1.84 (d, 3H), 1.08 (t, 6H).	639 [M+1]
I-330		4-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid		3 as in Example 211		406 [M+1]
I-331		4-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide	0.13	4	(300MHZ, CDCl3) δ 7.91 (s, 1H), 7.80 (d, 2H), 7.46 (d, 2H), 7.05 (m, 3H), 6.87 (m, 1H), 6.97 (q, 1H), 4.97 (s, 2H), 3.78 (m, 4H), 3.66 (m, 2H), 2.60 (m, 6H), 1.84 (m, 3H).	517 [M+1]
I-332		4-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(1-methyl-piperidin-4-yl)-benzamide	0.079	4 as in Example I-331	(300MHZ, CDCl3) δ 7.90 (s, 1H), 7.78 (d, 2H), 7.45 (d, 2H), 7.05 (m, 4H), 6.86 (q, 1H), 4.90 (s, 2H), 4.00 (m, 1H), 2.88 (m, 2H), 2.32 (s, 3H), 2.18 (m, 2H), 2.08 (m, 2H), 1.84 (d, 3H), 1.57 (m, 2H).	531 [M+1]
I-333		(4-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.057	4 as in Example I-331	(300MHZ, CDCl3) δ 7.90 (s, 1H), 7.54 (m, 2H), 7.42 (d, 2H), 7.05 (m, 3H), 5.86 (q, 1H), 4.88 (s, 2H), 3.80 (m, 2H), 3.74 (m, 4H), 1.84 (d, 3H), 1.57-2.18 (m, 11H)	541 [M+1]

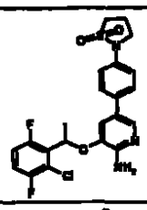
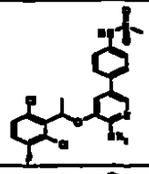
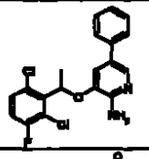
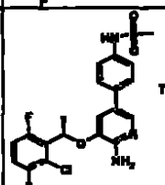
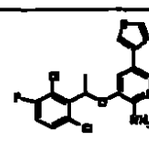
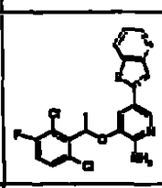
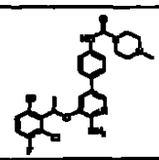
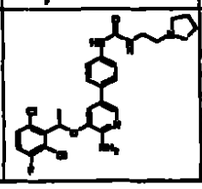
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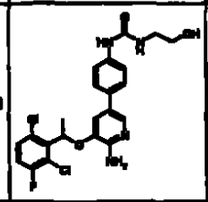
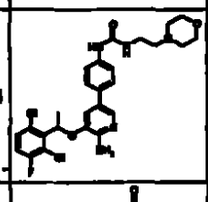
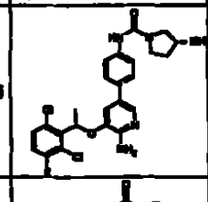
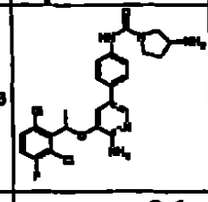
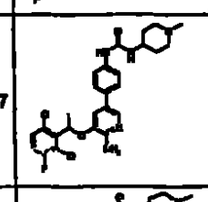
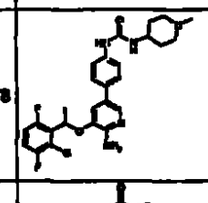
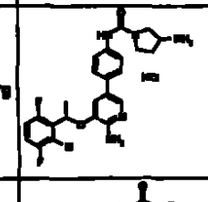
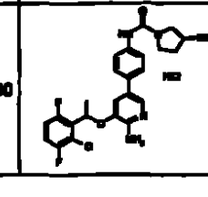
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS *m/z* (M+1)
I-334		(4-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone	0.089	4 as in Example I-331	(300MHZ, CDCl3) δ 7.68 (m, 6H), 7.25 (m, 3H), 6.27 (m, 1H), 4.88 (s, 2H), 3.78 (m, 5H), 3.31 (m, 2H), 2.44 (m, 1H), 2.17 (m, 1H), 1.83 (m, 3H).	473 [M+1]
I-335		(4-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone	0.09	4 as in Example I-331	(300MHZ, CDCl3) δ 7.90 (s, 1H), 7.42 (m, 4H), 7.05 (m, 3H), 5.97 (q, 1H), 4.86 (s, 2H), 4.62 (m, 1H), 3.65 (m, 1H), 2.86 (m, 2H), 2.68 (m, 1H), 2.41 (m, 1H), 1.84 (d, 3H), 1.84 (m, 1H), 1.05 (m, 6H).	501 [M+1]
I-336		4-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide	0.09	4 as in Example I-331	(300MHZ, CDCl3) δ 9.00 (s, 1H), 7.82 (s, 1H), 7.63 (d, 2H), 7.42 (d, 2H), 7.09 (m, 2H), 7.01 (m, 1H), 5.96 (q, 1H), 4.89 (s, 2H), 3.60 (m, 2H), 2.75 (m, 2H), 2.62 (m, 4H), 1.85 (m, 7H).	515 [M+1]
I-337		(4-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.09	4 as in Example I-331	(300MHZ, CDCl3) δ 7.90 (s, 1H), 7.63 (m, 2H), 7.45 (d, 2H), 7.05 (m, 3H), 5.99 (q, 1H), 4.86 (s, 2H), 4.45 (m, 1H), 3.69 (m, 2H), 3.00 (m, 4H), 1.84 (d, 3H), 1.70-2.18 (m, 10H)	541 [M+1]
I-338		(4-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone	0.077	4 as in Example I-331	(300MHZ, CDCl3) δ 7.90 (s, 1H), 7.44 (m, 4H), 7.07 (m, 3H), 5.95 (q, 1H), 4.87 (s, 2H), 3.60 (m, 4H), 2.43 (m, 4H), 2.33 (s, 3H), 1.84 (d, 3H).	487 [M+1]
I-339		(4-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.062	4 as in Example I-331	(300MHZ, CDCl3) δ 7.90 (s, 1H), 7.42 (m, 4H), 7.02 (m, 3H), 6.00 (q, 1H), 4.87 (s, 2H), 4.64 (m, 1H), 3.85 (m, 1H), 2.99 (m, 2H), 2.67 (m, 4H), 2.38 (m, 1H), 1.90 (m, 8H), 1.62 (m, 2H).	541 [M+1]
I-340		4-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide	0.086	4 as in Example I-331	(300MHZ, CDCl3) δ 7.91 (s, 1H), 7.86 (d, 2H), 7.45 (d, 2H), 7.10 (m, 3H), 7.01 (m, 1H), 5.96 (q, 1H), 4.90 (s, 2H), 3.60 (m, 2H), 2.80 (m, 2H), 2.58 (m, 4H), 1.85 (m, 7H).	501 [M+1]

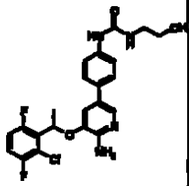
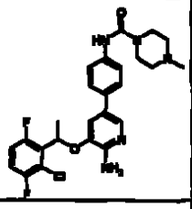
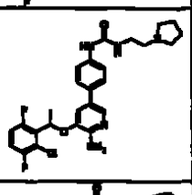
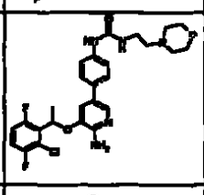
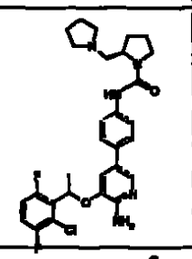
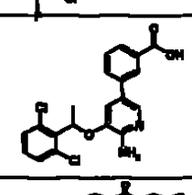
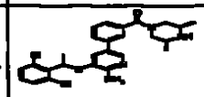
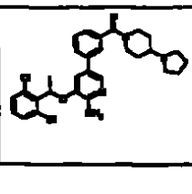
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-341		(4-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone	0.075	4 as in Example I-331	(300MHZ, CDCl3) δ 7.78 (s, 1H), 7.57 (m, 2H), 7.50 (d, 2H), 7.42 (s, 1H), 7.32 (m, 1H), 7.20 (m, 1H), 6.27 (m, 1H), 4.66 (s, 2H), 3.76 (m, 5H), 3.31 (m, 2H), 2.44 (m, 1H), 2.14 (m, 1H), 1.95 (m, 3H).	473 [M+1]
I-342		3-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid		as in Example 211		405 [M+1]
I-343		[3-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl]-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone	0.16	4	(300MHZ, CDCl3) δ 7.98 (s, 1H), 7.43 (m, 2H), 7.30 (m, 2H), 7.10 (m, 2H), 6.95 (m, 1H), 6.87 (q, 1H), 4.87 (s, 2H), 4.66 (m, 1H), 3.60 (m, 1H), 2.72 (m, 3H), 2.41 (m, 1H), 2.01 (s, 1H), 1.84 (d, 3H), 1.17 (m, 3H), 0.96 (m, 3H).	501 [M+1]
I-344		[3-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl]-((R)-3-amino-pyrrolidin-1-yl)-methanone	0.12	4 as in Example 343	(300MHZ, CDCl3) δ 7.85 (m, 5H), 7.42 (s, 1H), 7.32 (m, 1H), 7.20 (m, 1H), 6.27 (m, 1H), 4.85 (s, 2H), 3.75 (m, 5H), 3.31 (m, 2H), 2.44 (m, 1H), 2.16 (m, 1H), 1.93 (m, 3H).	473 [M+1]
I-345		3-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(1-methyl-piperidin-4-yl)-benzamide	0.2	4 as in Example 343	(300MHZ, CDCl3) δ 7.90 (s, 1H), 7.78 (s, 1H), 7.67 (d, 1H), 7.45 (m, 2H), 7.00 (m, 3H), 6.15 (bd, 1H), 5.98 (q, 1H), 4.08 (m, 1H), 2.97 (m, 2H), 2.36 (s, 3H), 2.27 (m, 2H), 2.10 (m, 2H), 1.84 (d, 3H), 1.74 (m, 2H).	501 [M+1]
I-346		[3-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl]-(4-methyl-piperazin-1-yl)-methanone	0.19	4 as in Example 343	(300MHZ, CDCl3) δ 7.86 (s, 1H), 7.42 (m, 3H), 7.30 (m, 2H), 7.09 (m, 2H), 7.00 (m, 1H), 6.95 (q, 1H), 4.87 (s, 2H), 3.63 (m, 2H), 3.47 (m, 2H), 2.51 (m, 2H), 2.33 (m, 5H), 1.84 (d, 3H).	487 [M+1]
I-347		3-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide	0.21	4 as in Example 343	(300MHZ, CDCl3) δ 8.69 (s, 1H), 7.91 (m, 2H), 7.85 (d, 1H), 7.42 (m, 2H), 7.00 (m, 3H), 6.99 (q, 1H), 4.85 (s, 2H), 3.60 (m, 2H), 2.78 (m, 2H), 2.63 (m, 4H), 1.84 (d, 3H), 1.77 (m, 6H).	515 [M+1]
I-348		3-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide	0.2	4 as in Example 343	(300MHZ, CDCl3) δ 7.91 (s, 1H), 7.86 (s, 1H), 7.70 (d, 1H), 7.50 (m, 2H), 7.00 (m, 4H), 6.99 (q, 1H), 4.86 (s, 2H), 3.60 (m, 2H), 2.78 (m, 2H), 2.63 (m, 4H), 1.86 (m, 7H).	501 [M+1]

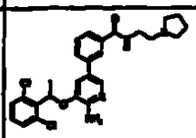
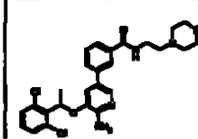
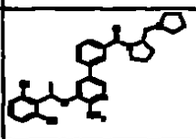
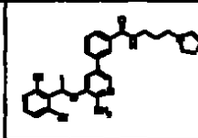
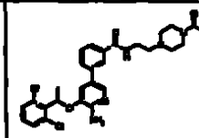
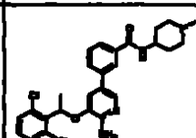
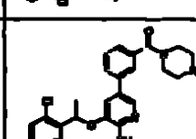
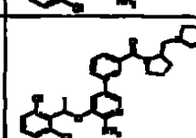
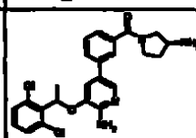
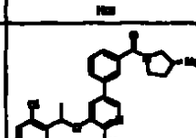
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-349		(3-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone	0.13	4 as in Example 343	(300MHZ, CDCl3) δ 7.70 (m, 6H), 7.42 (s, 1H), 7.26 (m, 1H), 7.20 (m, 1H), 6.27 (m, 1H), 4.85 (s, 2H), 3.75 (m, 5H), 3.31 (m, 2H), 2.66 (m, 1H), 2.44 (m, 1H), 1.93 (m, 3H).	473 [M+1]
I-350		3-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide	0.39	4 as in Example 343	(300MHZ, CDCl3) δ 7.91 (s, 1H), 7.84 (s, 1H), 7.65 (d, 1H), 7.46 (m, 2H), 7.06 (m, 3H), 6.83 (bs, 1H), 5.97 (q, 1H), 4.91 (s, 2H), 3.74 (m, 4H), 3.66 (m, 2H), 2.63 (m, 2H), 2.62 (m, 4H), 1.84 (m, 3H).	517 [M+1]
I-351		(3-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.23	4 as in Example 343	(300MHZ, CDCl3) δ 7.88 (s, 1H), 7.45 (m, 4H), 7.06 (m, 3H), 5.96 (q, 1H), 4.86 (s, 2H), 4.45 (m, 1H), 3.84 (m, 1H), 3.44 (m, 1H), 2.84 (m, 4H) 1.83 (d, 3H), 1.70-2.18 (m, 10H)	541 [M+1]
I-352		(3-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.15	4 as in Example 343	(300MHZ, CDCl3) δ 7.88 (s, 1H), 7.45 (m, 4H), 7.09 (m, 3H), 5.96 (q, 1H), 4.86 (s, 2H), 4.45 (m, 1H), 3.45 (m, 2H), 2.76 (m, 4H), 1.84 (d, 3H), 1.70-2.18 (m, 10H)	541 [M+1]
I-353		3-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine	0.23	3 as in Example 2		
I-354		3-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-5-[3-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine	0.22	3 as in Example 2		
I-355		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-pyridin-2-ylamine	0.066	3 as in Example 2	(400 MHz, DMSO-d6): d 7.74 (d, J = 2.0 Hz, 1H), 7.53 (m, 1H), 7.44 (m, 2H), 7.32 (d, J = 9.0 Hz, 2H), 7.00 (d, J = 8.6 Hz, 2H), 6.66 (d, J = 1.8 Hz, 1H), 6.11 (m, 1H), 5.79 (s, 2H), 4.30 (m, 2H), 3.5 (m, 6H), 1.90 (m, 4H), 1.807 (d, J = 6.7 Hz, 3H).	491 [M+1]
I-356		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-[2-(1-methyl-pyrrolidin-2-yl)-ethoxy]-phenyl]-pyridin-2-ylamine	0.079	3 as in Example 2	(400 MHz, DMSO-d6): d 7.73 (s, 1H), 7.54 (m, 1H), 7.44 (m, 2H), 7.284 (d, J = 8.2 Hz, 2H), 6.95 (d, J = 8.6 Hz, 2H), 6.68 (s, 1H, pyridine-H), 6.10 (m, 1H), 5.78 (s, 2H), 4.7 (m, 1H), 3.3 (m, 2H), 3.1 (m, 2H), 2.77 (s, 3H), 2.3 (m, 6H), 1.81 (d, J = 6.2 Hz, 3H).	504 [M+1]

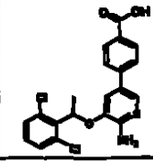
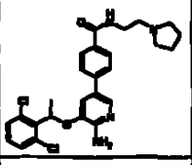
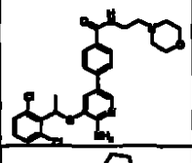
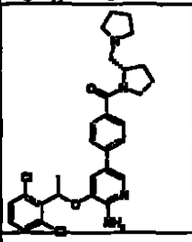
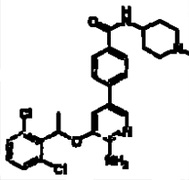
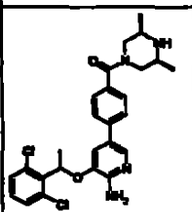
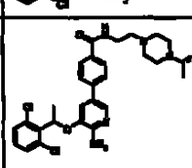
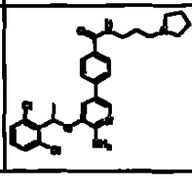
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-357		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine	0.13	3 as in Example 2	(400 MHz, DMSO-d6): d 7.72 (d, 1H), 7.53 (m, 1H), 7.44 (m, 1H), 7.33 (m, 2H), 7.03 (m, 3H), 6.23 (q, 1H), 4.35 (m, 2H), 3.95 (m, 1H), 3.0-3.8 (m, 8H), 1.861 (d, 3H).	505 [M+1]
I-358		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-[3-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine	0.22	3 as in Example I-2	(400 MHz, DMSO-d6): d 7.82 (d, 1H), 7.53 (q, 1H), 7.46 (t, 1H), 7.33 (t, 1H), 7.03 (m, 3H), 6.95 (dd, 1H), 6.24(q, 1H), 4.38 (m, 2H), 3.96 (m, 2H), 3.75 (m, 2H), 3.61(m, 2H), 3.5(m, 2H), 3.25(m, 2H), 1.861 (d, 3H).	505 [M+1]
I-359		1-(4-{6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenoxy)-3-morpholin-4-yl-propan-2-ol	0.045	3	(400 MHz, DMSO-d6): d 7.73 (d, J = 1.8 Hz, 1H), 7.56 (m, 1H), 7.44 (t, J = 8.8 Hz, 1H), 7.28 (d, J = 8.7 Hz, 2H), 6.94 (d, J = 8.8 Hz, 2H), 6.58 (d, J = 2.0 Hz, 1H), 6.11 (m, 1H), 5.75 (s, 2H), 4.88 (d, J = 2.0 Hz, 1H), 3.96 (m, 3H), 3.57 (t, J = 4.3 Hz, 4H), 2.42 (m, 6H), 1.81 (d, J = 6.7 Hz, 3H).	538 [M+1]
I-360		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(2-diethylamino-ethoxy)-phenyl]-pyridin-2-ylamine	0.033	3 as in Example 2	(400 MHz, DMSO-d6): d 7.73 (d, J = 1.8 Hz, 1H), 7.56 (m, 1H), 7.44 (t, J = 8.8 Hz, 1H), 7.28 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 6.58 (d, J = 1.8 Hz , 1H), 6.11 (m, 1H), 5.75 (s, 2H), 4.02 (t, J = 6.2 Hz, 2H), 2.756 (m, 2H), 2.55 (m, 4H), 1.81 (d, J = 6.7 Hz, 3H), 0.99 (t, J = 7.0 Hz , 6H).	464 [M+1]
I-361		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(1-methyl-piperidin-3-ylmethoxy)-phenyl]-pyridin-2-ylamine	0.043	3 as in Example 2	(400 MHz, DMSO-d6): d 7.73 (d, J = 2.0 Hz, 1H), 7.53 (m, 1H), 7.44 (t, J = 8.8 Hz, 1H), 7.27 (d, J = 8.7 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 6.57 (d, J = 1.8 Hz , 1H), 6.10 (m, 1H), 5.75 (s, 2H), 3.831(m, 2H), 2.81(m, 1H), 2.62 (s, 1H), 2.183 (s, 3H), 1.95 (m, 3H), 1.81 (d, J = 6.7 Hz, 3H), 1.72 (m, 4H).	504 [M+1]
I-362		5-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(2-diisopropylamino-ethoxy)-phenyl]-pyridin-2-ylamine	0.052	3 as in Example 2	(400 MHz, DMSO-d6): d 7.73 (d, J = 2.0 Hz, 1H), 7.53 (m, 1H), 7.44 (t, J = 8.8 Hz, 1H), 7.27 (m, 2H), 6.91 (m, 2H), 6.58 (d, J = 2.0 Hz , 1H), 6.11 (m, 1H), 5.74 (s, 2H), 3.68 (t, J = 6.7 Hz, 2H), 3.02 (m, 2H), 2.76 (t, J = 6.7 Hz, 2H), 1.81 (d, J = 6.7 Hz, 3H), 0.998 (m, 12H).	520 [M+1]
I-363		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(1-methyl-piperidin-4-yloxy)-phenyl]-pyridin-2-ylamine	0.052	3	(400 MHz, DMSO-d6): d 7.86 (d, J = 1.8 Hz, 1H), 7.49 (m, 1H), 7.377 (t, J = 8.2 Hz, 1H), 7.20 (m, 2H), 6.87 (m, 2H), 6.61 (d, J = 1.8 Hz , 1H), 6.04 (m, 1H), 5.69 (s, 2H), 4.30 (m, 1H), 2.55 (m, 2H), 2.12 (m, 5H), 1.84 (m, 2H), 1.74 (d, J = 6.7 Hz, 3H), 1.57 (m, 2H).	490 [M+1]
I-364		N-(4-{6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-methanesulfonamide	0.1	3 as in Example I-135		484 [M+1]

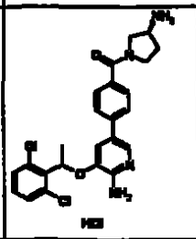
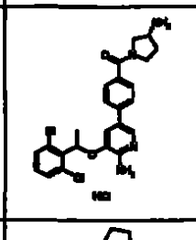
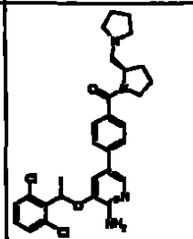
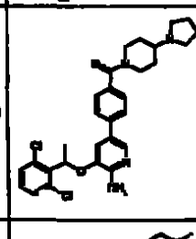
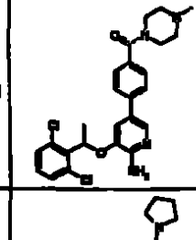
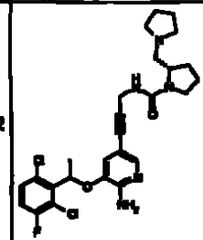
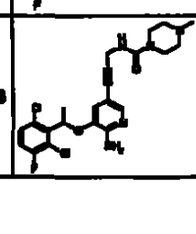
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-365		3-[1-(3-Chloro-3,6-difluoro-phenyl)-ethoxy]-5-[4-(1,1-dioxo-1lambda*6*-isothiazolidin-2-yl)-phenyl]-pyridin-2-ylamine	0.14	3 as in Example I-240		478 [M+1]
I-366		N-(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-methanesulfonamide	0.076	3 as in Example I-135	(300MHZ, CDCl3) δ 8.75 (s, 1H), 7.88(d, 1H), 7.55 (q, 1H), 7.45 (t, 1H), 7.35 (d, 2H), 7.18 (d, 2H), 6.9 (d, 1H), 6.10 (q, 1H), 5.85 (s, 2H), 2.99(s, 3H), 1.80 (d, 3H).	470 [M+1]
I-367		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-phenyl-pyridin-2-ylamine	0.5	3	(300MHZ, CDCl3) δ 7.80 (d, 1H), 7.65 (q, 1H), 7.45 (t, 1H), 7.35 (dd, 4H), 7.25 (m, 1H), 6.95 (d, 1H), 6.12 (q, 1H), 5.85 (s, 2H), 1.80 (d, 3H).	377 [M+1]
I-368	 TFA	N-(4-[6-Amino-5-[(R)-1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-methanesulfonamide	0.066	3 as in Example I-135	(300MHZ, CDCl3) δ 9.80 (s, 1H), 7.70(d, 1H), 7.49 (m, 3H), 7.30 (ddd, 1H), 7.25 (d, 1H), 7.18 (m, 2H), 6.10 (q, 1H), 2.95(s, 3H), 1.75 (d, 3H).	454 [M+1]
I-369		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-thiophen-3-yl-pyridin-2-ylamine	0.055	3		383 [M+1]
I-370		5-Benzo[b]thiophen-2-yl-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine	1.85	3		433 [M+1]
I-371		4-Methyl-piperazine-1-carboxylic acid (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.057	10	(300MHZ, CDCl3) δ 7.71 (s, 1H), 7.40 (d, 2H), 7.32-7.23 (m, 3H), 7.08 (t, 1H), 6.99 (s, 1H), 6.77 (bs, 1H), 6.11 (q, 1H), 5.82 (s, 2H), 3.60 (m, 4H), 2.67 (m, 4H), 2.40 (s, 3H), 1.87 (d, 3H).	518 [M+1]
I-372		1-(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-3-(2-pyrrolidin-1-yl-ethyl)-urea	0.21	10 as in Example I-371		532 [M+1]

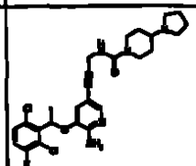
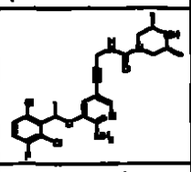
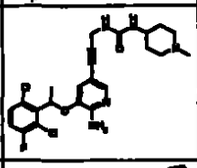
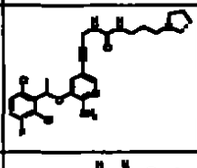
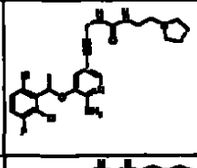
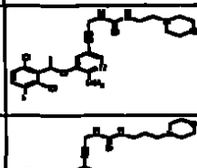
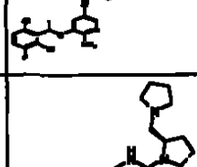
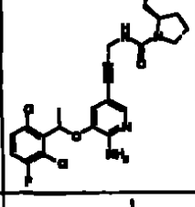
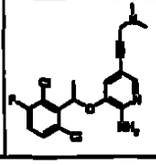
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS *m/z* (M+1)
I-373		1-(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-3-(2-hydroxy-ethyl)-urea	0.084	10 as in Example I-371	(300MHZ, CDCl3) δ 7.68 (s, 2H), 7.45 (m, 2H), 7.36 (d, 2H), 7.25 (m, 2H), 6.95 (s, 2H), 6.55 (q, 1H), 4.88 (s, 2H), 3.83 (t, 2H), 3.31 (m, 3H), 1.87 (d, 3H).	479 [M+1]
I-374		1-(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-3-(2-morpholin-4-yl-ethyl)-urea	0.082	10 as in Example I-371	(300MHZ, CDCl3) δ 7.68 (s, 1H), 7.55 (m, 3H), 7.35 (d, 2H), 7.23 (m, 3H), 6.95 (s, 1H), 6.55 (q, 1H), 4.89 (s, 2H), 3.71 (t, 2H), 3.31 (m, 6H), 2.51 (m, 4H), 1.88 (d, 3H).	548.2 [M+1]
I-375		(R)-3-Amino-pyrrolidine-1-carboxylic acid (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.063	10 as in Example I-371	(300MHZ, CDCl3) δ 7.66 (m, 4H), 7.31 (m, 3H), 7.19 (m, 2H), 6.57 (m, 1H), 4.57 (s, 2H), 3.95 (m, 1H), 3.80 (m, 1H), 3.60 (m, 2H), 3.31 (m, 2H), 2.48 (m, 1H), 2.18 (m, 1H), 1.86 (d, 3H).	503.8 [M+1]
I-376		(S)-3-Amino-pyrrolidine-1-carboxylic acid (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.052	10 as in Example I-371	(300MHZ, CDCl3) δ 7.66 (m, 4H), 7.31 (m, 3H), 7.19 (m, 2H), 6.57 (m, 1H), 4.57 (s, 2H), 3.95 (m, 1H), 3.80 (m, 1H), 3.60 (m, 2H), 3.31 (m, 2H), 2.48 (m, 1H), 2.18 (m, 1H), 1.86 (d, 3H).	504.1 [M+1]
I-377		1-(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-3-(1-methyl-piperidin-4-yl)-urea	0.04	10 as in Example I-371		534 [M+1]
I-378		1-(4-[6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-3-(1-methyl-piperidin-4-yl)-urea	0.038	10 as in Example I-371		518 [M+1]
I-379		(R)-3-Amino-pyrrolidine-1-carboxylic acid (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.089	10 as in Example I-371		488 [M+1]
I-380		(S)-3-Amino-pyrrolidine-1-carboxylic acid (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide	0.075	10 as in Example I-371		488 [M+1]

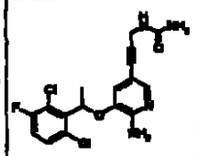
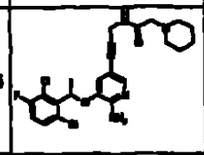
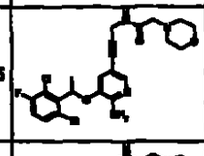
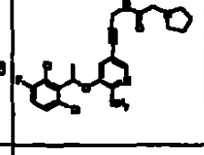
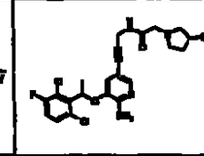
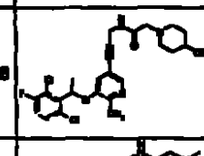
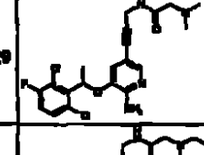
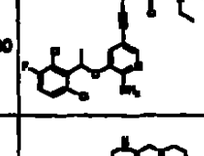
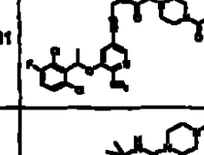
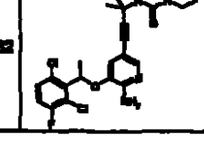
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-381		1-(4-{6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(2-hydroxy-ethyl)-urea	0.11	10 as in Example I-371	(300MHZ, CDCl3) δ 7.69 (d, 2H), 7.37 (d, 2H), 7.25 (d, 2H), 7.15 (m, 2H), 7.09 (d, 2H), 6.00 (q, 1H), 4.66 (s, 2H), 3.63 (t, 2H), 3.32 (m, 3H), 1.89 (d, 3H).	463 [M+1]
I-382		4-Methyl-piperazine-1-carboxylic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide	0.082	10 as in Example I-371	(300MHZ, CDCl3) δ 7.78 (s, 1H), 7.41 (d, 2H), 7.29 (d, 2H), 7.09 (s, 1H), 7.05 (m, 1H), 6.95 (m, 1H), 6.59 (bs, 1H), 6.00 (q, 1H), 5.25 (s, 2H), 3.58 (m, 4H), 2.83 (m, 4H), 2.38 (s, 3H), 1.84 (d, 3H).	502 [M+1]
I-383		1-(4-{6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(2-pyrrolidin-1-yl-ethyl)-urea	0.11	10 as in Example I-371		516 [M+1]
I-384		1-(4-{6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(2-morpholin-4-yl-ethyl)-urea	0.13	10 as in Example I-371	(300MHZ, CDCl3) δ 7.83 (d, 1H), 7.29 (m, 5H), 7.00 (m, 4H), 5.94 (q, 1H), 4.57 (bs, 2H), 3.67 (m, 4H), 3.38 (m, 2H), 2.62 (m, 4H), 1.86 (d, 3H).	533.7 [M+1]
I-385		(R)-2-Pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide	0.10	10 as in Example I-371	(300MHZ, CDCl3) δ 7.93 (s, 1H), 7.67 (d, 2H), 7.27 (d, 2H), 6.98 (m, 4H), 6.70 (q, 1H), 4.84 (s, 2H), 3.85 (m, 1H), 3.75 (m, 1H), 3.40 (m, 1H), 2.90 (m, 4H), 2.65 (m, 4H), 2.10 (m, 3H), 1.85 (d, 3H), 1.9-1.7 (m, 3H).	555.8 [M+1]
I-386		3-{6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-benzoic acid		3 as in Example I-211		403 [M+1]
I-387		(3-{6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone	0.16	4	(300MHZ, CDCl3) δ 7.86 (s, 1H), 7.39 (m, 4H), 7.31 (d, 2H), 7.15 (t, 1H), 7.02 (s, 1H), 6.15 (m, 1H), 4.93 (s, 2H), 4.85 (m, 1H), 3.56 (m, 1H), 2.95 (m, 1H), 2.79 (m, 1H), 2.71 (m, 1H), 2.44 (m, 1H), 1.84 (d, 3H), 1.85 (m, 1H), 1.25 (d, 3H), 1.17 (d, 3H).	501 [M+1]
I-388		(3-{6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.1	4 as in Example I-387	(300MHZ, CDCl3) δ 7.86 (s, 1H), 7.38 (m, 4H), 7.32 (d, 2H), 7.15 (t, 1H), 7.02 (s, 1H), 6.15 (m, 1H), 4.90 (s, 2H), 4.85 (m, 1H), 3.85 (m, 1H), 3.05 (m, 2H), 2.80 (m, 1H), 2.85 (m, 4H), 2.30 (m, 1H), 2.05 (m, 1H), 1.88 (d, 3H), 1.81 (m, 3H), 1.52 (m, 4H).	539 [M+1]

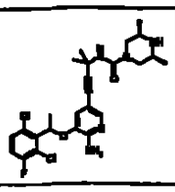
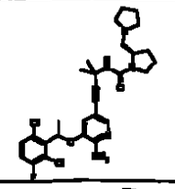
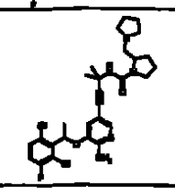
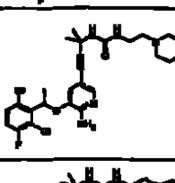
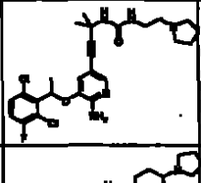
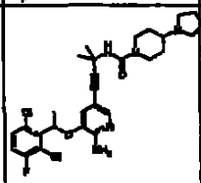
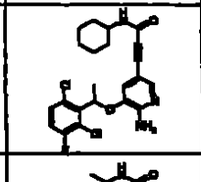
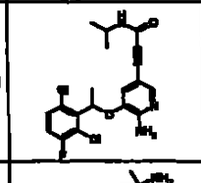
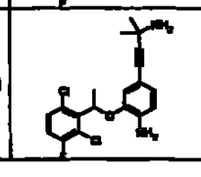
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-389		3-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide	0.13	4 as in Example I-387	(300MHZ, CDCl3) δ 7.86 (s, 1H), 7.82 (s, 1H), 7.69 (d, 1H), 7.45 (m, 3H), 7.32 (d, 2H), 7.15 (t, 1H), 7.08 (s, 1H), 6.86 (bm, 1H), 6.16 (q, 1H), 4.93 (s, 2H), 3.81 (m, 2H), 2.78 (m, 2H), 2.63 (m, 4H), 1.87 (d, 3H), 1.82 (m, 4H).	501 [M+1]
I-390		3-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide	0.12	4 as in Example I-387	(300MHZ, CDCl3) δ 7.89 (s, 1H), 7.82 (s, 1H), 7.65 (d, 1H), 7.46 (m, 3H), 7.32 (d, 2H), 7.15 (t, 1H), 7.08 (s, 1H), 6.78 (bm, 1H), 6.16 (q, 1H), 4.85 (s, 2H), 3.73 (m, 4H), 3.69 (m, 2H), 2.62 (m, 2H), 2.51 (m, 4H), 1.87 (d, 3H).	517 [M+1]
I-391		(3-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.086	4 as in Example I-387	(300MHZ, CDCl3) δ 7.86 (d, 1H), 7.37 (m, 4H), 7.30 (d, 2H), 7.15 (t, 1H), 7.02 (s, 1H), 6.15 (m, 1H), 4.91 (s, 2H), 4.45 (m, 1H), 3.41 (m, 2H), 2.70 (m, 4H), 1.84 (d, 3H), 1.70-2.0 (m, 10H)	541[M+1]
I-392		3-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide	0.072	4 as in Example I-387	(300MHZ, CDCl3) δ 8.60 (bm, 1H), 7.89 (s, 1H), 7.85 (d, 1H), 7.45 (m, 3H), 7.32 (d, 2H), 7.15 (t, 1H), 7.04 (s, 1H), 6.17 (q, 1H), 4.89 (s, 2H), 3.62 (m, 2H), 2.79 (m, 2H), 2.66 (m, 4H), 1.88 (d, 3H), 1.83 (m, 2H), 1.78 (m, 4H).	513 [M+1]
I-393		N-[2-(4-Acetyl-piperazin-1-yl)-ethyl]-3-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-benzamide	0.079	4 as in Example I-387	(300MHZ, CDCl3) δ 7.88 (s, 1H), 7.81 (s, 1H), 7.63 (d, 1H), 7.46 (m, 3H), 7.32 (d, 2H), 7.15 (t, 1H), 7.06 (s, 1H), 6.68 (bm, 1H), 6.16 (q, 1H), 4.94 (s, 2H), 3.65 (m, 4H), 3.50 (m, 2H), 2.62 (m, 2H), 2.52 (m, 4H), 2.09 (s, 3H), 1.87 (d, 3H).	555 [M+1]
I-394		3-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-N-(1-methyl-piperidin-4-yl)-benzamide	0.061	4 as in Example I-387	(300MHZ, CDCl3) δ 7.89 (s, 1H), 7.73 (s, 1H), 7.65 (d, 1H), 7.50(d, 1H), 7.43 (t, 1H), 7.32 (d, 2H), 7.16 (t, 1H), 7.04 (s, 1H), 6.15 (m, 1H), 6.08 (bd, 1H), 4.82 (s, 2H), 4.03 (m, 1H), 2.94 (m, 2H), 2.38 (s, 3H), 2.28 (m, 2H), 2.09 (m, 2H), 1.88 (d, 3H), 1.70 (m, 2H).	499 [M+1]
I-395		(3-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone	0.058	4 as in Example I-387	(300MHZ, CDCl3) δ 7.50 (s, 1H), 7.40 (m, 4H), 7.30 (d, 2H), 7.16 (t, 1H), 7.02 (s, 1H), 6.15 (m, 1H), 4.93 (s, 2H), 3.82 (m, 2H), 3.45 (m, 2H), 2.52 (m, 2H), 2.38 (m, 2H), 2.33 (s, 3H), 1.88 (d, 2H).	487 [M+1]
I-396		(3-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.16	4 as in Example I-387	(300MHZ, CDCl3) δ 7.86 (d, 1H), 7.37 (m, 4H), 7.30 (d, 2H), 7.15 (t, 1H), 7.02 (s, 1H), 6.15 (m, 1H), 4.91 (s, 2H), 4.45 (m, 1H), 3.41 (m, 2H), 2.70 (m, 4H), 1.84 (d, 3H), 1.70-2.0 (m, 10H)	541 [M+1]
I-397		(3-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone	0.055	4 as in Example I-387	(300MHZ, CD3OD) δ 7.74 (s, 1H), 7.69-7.43 (m, 6H), 7.32 (t, 1H), 7.22 (s, 1H), 6.42 (m, 1H), 4.05-3.80 (m, 4H), 3.50 (m, 1H), 2.80 (m, 1H), 2.18 (m, 1H), 1.90 (d, 3H).	471 [M+1]
I-398		(3-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone	0.072	4 as in Example I-387	(300MHZ, CD3OD) δ 7.74 (s, 1H), 7.69-7.43 (m, 6H), 7.32 (t, 1H), 7.22 (s, 1H), 6.42 (m, 1H), 4.05-3.80 (m, 4H), 3.50 (m, 1H), 2.80 (m, 1H), 2.18 (m, 1H), 1.90 (d, 3H).	471 [M+1]

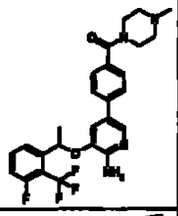
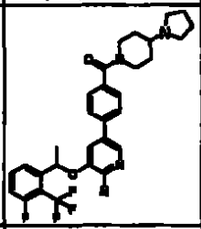
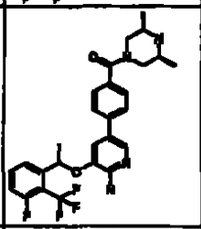
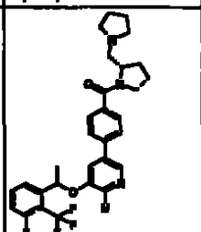
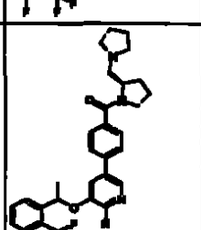
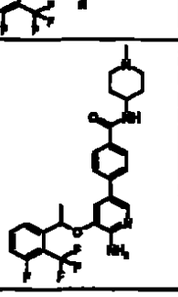
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-399		4-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid		3 as in Example I-211		403 [M+1]
I-400		4-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide	0.089	4	(300MHZ, CDCl3) δ 7.89 (s, 1H), 7.79 (d, 2H), 7.43 (d, 2H), 7.32 (d, 2H), 7.15 (t, 1H), 7.02 (s, 1H), 6.87 (bm, 1H), 6.15 (q, 1H), 4.93 (s, 2H), 3.66 (m, 2H), 2.72 (m, 2H), 2.56 (m, 4H), 1.87 (d, 3H), 1.80 (m, 4H).	501[M+1]
I-401		4-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide	0.073	4 as in Example I-400	(300MHZ, CDCl3) δ 7.90 (s, 1H), 7.79 (d, 2H), 7.44 (d, 2H), 7.32 (d, 2H), 7.16 (t, 1H), 7.03 (s, 1H), 6.77 (bm, 1H), 6.15 (q, 1H), 4.95 (s, 2H), 3.74 (m, 4H), 3.57 (m, 2H), 2.61 (m, 2H), 2.52 (m, 4H), 1.87 (d, 3H).	515 [M+1]
I-402		(4-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.069	4 as in Example I-400	(300MHZ, CDCl3) δ 7.87 (s, 1H), 7.52 (m, 2H), 7.39 (d, 2H), 7.31 (d, 2H), 7.15 (t, 1H), 7.01 (s, 1H), 6.15 (q, 1H), 4.91 (s, 2H), 4.45 (m, 1H), 3.41 (m, 2H), 2.70 (m, 4H), 1.86 (d, 3H), 1.70-2.0 (m, 10H)	639 [M+1]
I-403		4-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-N-(1-methyl-piperidin-4-yl)-benzamide	0.082	4 as in Example I-400	(300MHZ, CDCl3) δ 7.89 (s, 1H), 7.78 (d, 2H), 7.42 (d, 2H), 7.31 (d, 2H), 7.15 (t, 1H), 7.02 (s, 1H), 6.15 (q, 1H), 6.97 (bd, 1H), 4.94 (s, 2H), 4.03 (m, 1H), 2.85 (m, 2H), 2.32 (s, 3H), 2.18 (m, 2H), 2.05 (m, 2H), 1.86 (d, 3H), 1.80 (m, 2H).	501[M+1]
I-404		(4-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone	0.052	4 as in Example I-400	(300MHZ, CDCl3) δ 7.88 (s, 1H), 7.41 (m, 4H), 7.32 (d, 2H), 7.15 (t, 1H), 7.02 (s, 1H), 6.15 (q, 1H), 4.92 (s, 2H), 4.62 (m, 1H), 3.66 (m, 1H), 2.82 (m, 2H), 2.68 (m, 1H), 2.40 (m, 1H), 1.87 (d, 3H), 1.69 (m, 1H), 1.15 (d, 3H), 0.98 (d, 3H).	499 [M+1]
I-405		N-[2-(4-Acetyl-piperazin-1-yl)-ethyl]-4-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-benzamide	0.082	4 as in Example I-400	(300MHZ, CDCl3) δ 7.90 (s, 1H), 7.78 (d, 2H), 7.44 (d, 2H), 7.32 (d, 2H), 7.15 (t, 1H), 7.03 (s, 1H), 6.89 (bm, 1H), 6.15 (q, 1H), 4.95 (s, 2H), 3.68 (m, 2H), 3.61 (m, 2H), 3.50 (m, 2H), 2.62 (m, 2H), 2.52 (m, 4H), 2.10 (s, 3H), 1.87 (d, 3H).	558 [M+1]
I-406		4-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide	0.081	4 as in Example I-400	(300MHZ, CDCl3) δ 8.80 (bm, 1H), 7.90 (s, 1H), 7.79 (d, 2H), 7.40 (d, 2H), 7.31 (d, 2H), 7.15 (t, 1H), 7.02 (s, 1H), 6.15 (q, 1H), 4.91 (s, 2H), 3.62 (m, 2H), 2.78 (m, 2H), 2.66 (m, 4H), 1.87 (d, 3H), 1.85 (m, 4H), 1.26 (m, 2H).	513 [M+1]

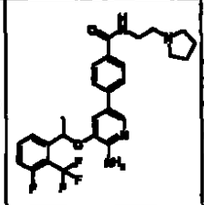
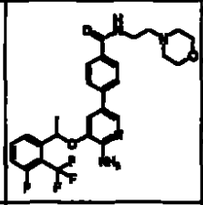
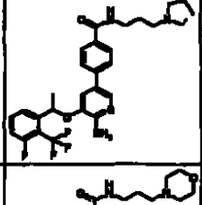
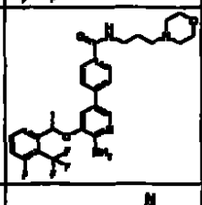
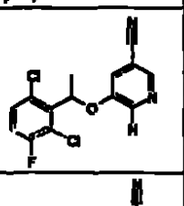
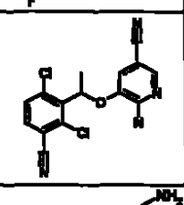
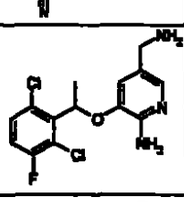
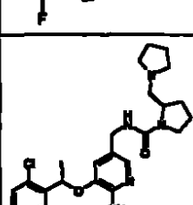
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-407		(4-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-3-aminopyrrolidin-1-yl)-methanone	0.06	4 as in Example I-400	(300MHZ, CD3OD) δ 7.74-7.24 (m, 9H), 6.39 (m, 1H), 4.05-3.80 (m, 4H), 3.50 (m, 1H), 2.80 (m, 1H), 2.15 (m, 1H), 1.90 (d, 3H).	471 [M+1]
I-408		(4-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone	0.049	4 as in Example I-400	(300MHZ, CD3OD) δ 7.74-7.24 (m, 9H), 6.39 (m, 1H), 4.05-3.80 (m, 4H), 3.50 (m, 1H), 2.80 (m, 1H), 2.15 (m, 1H), 1.90 (d, 3H).	471 [M+1]
I-409		(4-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.081	4 as in Example I-400	(300MHZ, CDCl3) δ 7.87 (s, 1H), 7.82 (m, 2H), 7.39 (d, 2H), 7.31 (d, 2H), 7.15 (t, 1H), 7.01 (s, 1H), 6.15 (q, 1H), 4.91 (s, 2H), 4.45 (m, 1H), 3.41 (m, 2H), 2.70 (m, 4H), 1.86 (d, 3H), 1.70-2.0 (m, 10H)	539 [M+1]
I-410		(4-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.055	4 as in Example I-400	(300MHZ, CDCl3) δ 7.87 (s, 1H), 7.38 (m, 4H), 7.32 (d, 2H), 7.17 (t, 1H), 7.01 (s, 1H), 6.15 (q, 1H), 4.91 (s, 2H), 4.60 (m, 1H), 3.78 (m, 1H), 3.00 (m, 2H), 2.60 (m, 4H), 2.28 (m, 1H), 1.95 (m, 2H), 1.86 (d, 3H), 1.81 (m, 4H), 1.58 (m, 2H).	541[M+1]
I-411		(4-[6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone	0.093	4 as in Example I-400	(300MHZ, CDCl3) δ 7.87 (s, 1H), 7.40 (m, 4H), 7.31 (d, 2H), 7.16 (t, 1H), 7.01 (s, 1H), 6.15 (q, 1H), 4.92 (s, 2H), 3.78 (m, 2H), 3.52 (m, 2H), 2.41 (m, 4H), 2.34 (s, 3H), 1.86 (d, 3H).	457 [M+1]
I-412		(S)-2-Pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl) -amide	0.057	11	(300MHZ, CDCl3) δ 9.05(br, 1H), 7.70 (s, 1H), 7.06 (t, 1H), 6.70 (s, 1H), 6.02 (q, 1H), 5.01 (s, 2H), 4.15 (dd, 2H), 3.75 (m, 2H), 3.25(m, 1H), 2.75 (m, 3H), 2.45 (m, 3H), 2.06 (m, 1H), 1.78 (d, 3H), 1.68 (br, 7H).	534 [M+1]
I-413		4-Methyl-piperazine-1-carboxylic acid (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-amide	0.058	11	(300MHZ, CDCl3) δ 7.75(s, 1H), 7.30 (m, 2H), 7.05 (t, 1H), 6.75 (s, 1H), 6.02 (q, 1H), 5.01 (s, 2H), 4.20 (d, 2H), 3.45 (m, 4H), 2.48 (m, 4H), 2.29 (s, 3H), 1.81 (d, 3H).	480 [M+1]

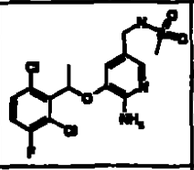
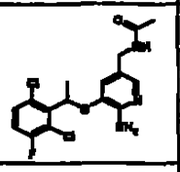
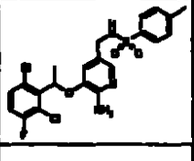
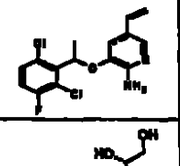
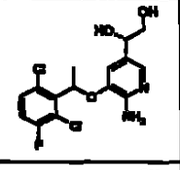
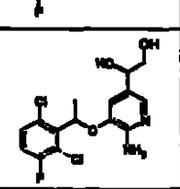
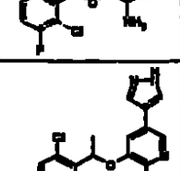
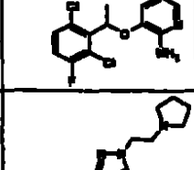
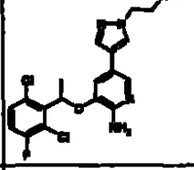
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-414		4-Pyrrolidin-1-yl-piperidine-1-carboxylic acid (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-amide	0.058	11	(300MHZ, CDCl3) δ 7.75(s, 1H), 7.30 (m, 2H), 7.10 (t, 1H), 6.70 (s, 1H), 6.02 (q, 1H), 5.01 (s, 2H), 4.20 (d, 2H), 3.80(d, 1H) 2.69 (t, 2H), 2.55 (s, 4H), 2.21 (m, 2H), 1.80(d, 2H),1.81 (d, 3H), 1.45(m, 2H), 1.25(m, 2H).	534 [M+1]
I-415		(3R,5S)-3,5-Dimethyl-piperazine-1-carboxylic acid (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy] -pyridin-3-yl]-prop-2-ynyl)-amide	0.083	11	(300MHZ, CDCl3) δ 7.75(s, 1H), 7.30 (m, 2H), 7.05 (t, 1H), 6.78 (s, 1H), 6.02 (q, 1H), 5.01 (s, 2H), 4.78(s, 1H), 4.20 (d, 2H), 3.85 (d, 1H), 2.85(m, 4H), 2.45 (t, 1H), 1.89 (s, 3H), 1.01 (d, 6H).	494 [M+1]
I-416		1-(3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-3-(1-methyl-piperidin-4-yl)-urea	0.051	11	(300MHZ, CDCl3) δ 7.75(s, 1H), 7.30 (m, 2H), 7.05 (t, 1H), 6.70 (s, 1H), 6.00 (q, 1H), 5.25(m, 1H), 5.05 (s, 2H), 4.80(d, 1H), 4.18 (d, 2H), 2.75 (d, 2H), 2.20(s, 3H), 2.10 (t, 2H), 1.85(d, 2H), 1.75 (d, 3H), 1.45 (d, 2H).	494 [M+1]
I-417		1-(3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-3-(3-pyrrolidin-1-yl-propyl)-urea	0.062	11	(300MHZ, CDCl3) δ 7.70(s, 1H), 7.30 (m, 2H), 7.05 (t, 1H), 6.70 (s, 1H), 6.00 (q, 1H), 5.30(m, 1H), 5.01 (s, 2H), 4.15 (d, 2H), 3.25 (m, 2H), 2.80(m, 6H), 1.80(d, 3H), 1.82 (m, 4H), 1.80 (m, 2H).	508 [M+1]
I-418		1-(3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-3-(2-pyrrolidin-1-yl-ethyl)-urea	0.052	11	(300MHZ, CDCl3) δ 7.70(s, 1H), 7.30 (m, 2H), 7.05 (t, 1H), 6.70 (s, 1H), 6.00 (q, 1H), 5.45(s, 1H), 5.15 (s, 2H), 4.15 (d, 2H), 3.25 (m, 2H), 2.60(t, 2H), 2.80(m, 4H), 1.80(d, 3H), 1.70 (s, 4H).	494 [M+1]
I-419		1-(3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-3-(2-morpholin-4-yl-ethyl)-urea	0.055	11	(300MHZ, CDCl3) δ 7.73(s, 1H), 7.28 (m, 2H), 7.05 (t, 1H), 6.70 (s, 1H), 6.00 (q, 1H), 5.25(s, 1H), 5.15 (s, 2H), 4.15 (d, 2H), 3.85 (m, 4H), 3.25(m, 2H), 2.45(m, 6H), 1.80(d, 3H).	510 [M+1]
I-420		1-(3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-3-(3-morpholin-4-yl-propyl)-urea	0.064	11	(300MHZ, CDCl3) δ 7.70(s, 1H), 7.30 (m, 2H), 7.05 (t, 1H), 6.70 (s, 1H), 6.00 (q, 1H), 5.10(s, 2H), 4.15 (d, 2H), 3.70 (m, 6H), 3.20(s, 2H), 2.50(m, 4H), 1.80(d, 3H), 1.65(m, 2H).	524 [M+1]
I-421		(R)-2-Pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl) -amide	0.071	11	(300MHZ, CDCl3) δ 9.05(br, 1H), 7.70 (s, 1H), 7.05 (t, 1H), 6.70 (s, 1H), 6.02 (q, 1H), 5.01 (s, 2H), 4.15 (dd, 2H), 3.75 (m, 2H), 3.25(m, 1H), 2.75 (m, 3H), 2.45 (m, 3H), 2.05 (m, 1H), 1.78 (d, 3H), 1.65 (br, 7H).	534 [M+1]
I-422		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-dimethylamino-prop-1-ynyl)-pyridin-2-ylamine	0.071	11		382 [M+1]

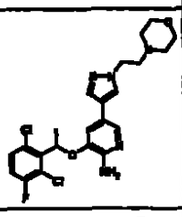
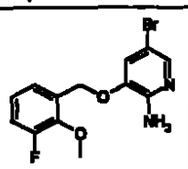
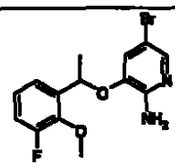
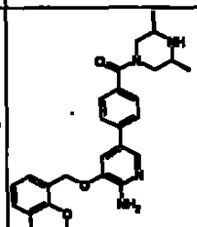
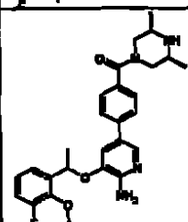
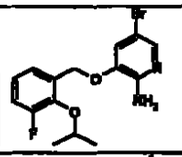
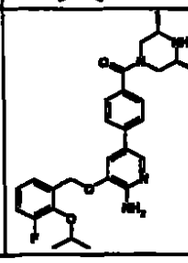
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS *m/z* (M+1)
I-423		(3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-urea	0.092	11		397 [M+1]
I-424		N-(3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-2-piperidin-1-yl-acetamide	0.016	12	(300MHZ, CDCl3) δ 7.74 (s, 1H), 7.45 (bm, 1H), 7.31 (dd, 1H), 7.07 (t, 1H), 6.73 (s, 1H), 6.00 (q, 1H), 4.99 (s, 2H), 4.28 (d, 2H), 2.88(s, 2H), 2.46 (m, 4H), 1.91 (d, 3H), 1.59 (m, 4H), 1.45 (m, 2H).	579 [M+1]
I-425		N-(3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-2-morpholin-4-yl-acetamide	0.027	12	(300MHZ, CDCl3) δ 7.74 (s, 1H), 7.45 (bm, 1H), 7.31 (m, 2H), 7.08 (t, 1H), 6.71 (s, 1H), 6.00 (q, 1H), 5.02 (s, 2H), 4.27 (d, 2H), 3.73 (m, 4H), 3.06 (s, 2H), 2.54 (m, 4H), 1.91 (d, 3H).	481 [M+1]
I-426		N-(3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-2-pyrrolidin-1-yl-acetamide	<0.0091	12	(300MHZ, CDCl3) δ 7.74 (s, 1H), 7.37 (bm, 1H), 7.31 (dd, 1H), 7.08 (t, 1H), 6.72 (s, 1H), 6.00 (q, 1H), 5.01 (s, 2H), 4.27 (d, 2H), 3.18 (s, 2H), 2.63 (m, 4H), 2.01 (m, 2H), 1.81 (d, 3H), 1.80 (m, 2H).	466 [M+1]
I-427		N-(3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-2-((R)-3-hydroxy-pyrrolidin-1-yl)-acetamide	0.011	12	(300MHZ, CDCl3) δ 7.71 (s, 1H), 7.45 (bm, 1H), 7.31 (dd, 1H), 7.07 (t, 1H), 6.72 (s, 1H), 5.99 (q, 1H), 5.05 (s, 2H), 4.42 (m, 1H), 4.25 (m, 2H), 3.21 (s, 2H), 3.00 (m, 1H), 2.80 (m, 1H), 2.71 (m, 1H), 2.45 (m, 1H), 2.22 (m, 1H), 1.79 (d, 3H), 1.76 (m, 2H).	481 [M+1]
I-428		N-(3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-2-(4-hydroxy-piperidin-1-yl)-acetamide	0.012	12	(300MHZ, CDCl3) δ 7.73 (d, 1H), 7.38 (bm, 1H), 7.31 (dd, 1H), 7.08 (dd, 1H), 6.72 (d, 1H), 6.00 (q, 1H), 5.03 (s, 2H), , 4.29 (d, 2H), 3.74 (m, 1H), 3.02 (s, 2H), 2.76 (m, 2H), 2.32 (m, 2H), 1.82 (m, 4H), 1.80 (d, 3H).	495 [M+1]
I-429		N-(3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-2-dimethylamino-acetamide	0.022	12	(200MHZ, CDCl3) δ 7.73 (d, 1H), 7.38 (bm, 1H), 7.31 (dd, 1H), 7.08 (dd, 1H), 6.72 (d, 1H), 6.00 (q, 1H), 4.99 (s, 2H), 4.28 (d, 2H), 2.98 (s, 2H), 2.31 (s, 6H), 1.80 (d, 3H).	439 [M+1]
I-430		N-(3-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-2-diethylamino-acetamide	0.013	12	(300MHZ, CDCl3) δ 7.73 (d, 1H), 7.59 (bm, 1H), 7.30 (dd, 1H), 7.07 (dd, 1H), 6.72 (d, 1H), 6.00 (q, 1H), 4.99 (s, 2H), 4.25 (d, 2H), 3.05 (s, 2H), 2.57 (dd, 4H), 1.80 (d, 3H), 1.03 (t, 6H).	467 [M+1]
I-431		2-(4-Acetyl-piperazin-1-yl)-N-(3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]pyridin-3-yl]-prop-2-ynyl)-acetamide	0.027	12	(300MHZ, CDCl3) δ 7.73 (d, 1H), 7.31 (dd, 1H), 7.25 (bm, 1H), 7.08 (dd, 1H), 6.71 (d, 1H), 6.00 (q, 1H), 5.04 (s, 2H), , 4.27 (d, 2H), 3.66 (m, 2H), 3.52 (m, 2H), 3.08 (s, 2H), 2.78 (m, 2H), 2.32 (m, 2H), 2.63 (m, 4H), 2.10 (s, 3H), 1.81 (d, 3H).	522 [M+1]
I-432		4-Methyl-piperazine-1-carboxylic acid (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-1,1-dimethyl-prop-2-ynyl)-amide	Id 0.61	13 as in Example I-412	(300MHZ, CDCl3) δ 7.73 (d, 1H), 7.30 (dd, 1H), 7.07 (t, 1H), 6.75 (d, 1H), 6.01 (q, 1H), 5.01 (s, 2H), 4.64 (s, 1H), 3.38 (m, 4H), 2.42 (m, 4H), 2.31 (s, 3H), 1.79 (d, 3H), 1.70 (s, 6H).	508 [M+1]

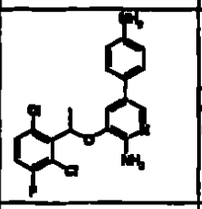
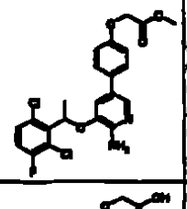
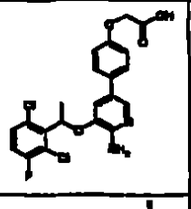
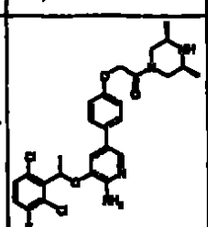
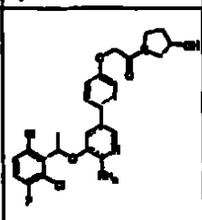
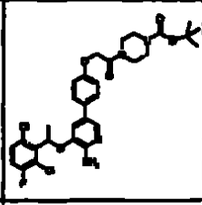
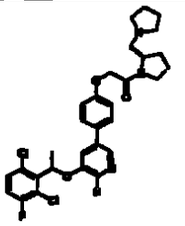
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-433		(3R,5S)-3,5-Dimethyl-piperazine-1-carboxylic acid (3-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy] -pyridin-3-yl]-1,1-dimethyl-prop-2-ynyl)-amide	KI 1.5	11	(300MHZ, CDCl3) δ 7.74 (s, 1H), 7.30 (dd, 1H), 7.07 (t, 1H), 6.79 (s, 1H), 6.01 (q, 1H), 4.93 (s, 2H), 4.89 (s, 1H), 3.75 (m, 2H), 2.82 (m, 2H), 2.38 (m, 2H), 1.90 (d, 3H), 1.71 (s, 6H), 1.09 (d, 6H).	522 [M+1]
I-434		(R)-2-Pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (3-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-1,1-dimethyl-prop-2-ynyl)-amide	KI 1.22	11	(300MHZ, CDCl3) δ 8.44 (bs, 1H), 7.72 (d, 1H), 7.30 (dd, 1H), 7.07 (t, 1H), 6.79 (s, 1H), 6.01 (q, 1H), 4.87 (s, 2H), 3.75 (m, 1H), 3.25 (m, 1H), 2.68 (m, 2H), 2.59 (m, 2H), 2.40 (m, 1H), 2.05 (m, 1H), 1.82-1.68 (m, 17H), 1.56 (m, 1H).	562 [M+1]
I-435		(S)-2-Pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (3-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-1,1-dimethyl-prop-2-ynyl)-amide	KI 1.58	11	(300MHZ, CDCl3) δ 8.44 (bs, 1H), 7.72 (s, 1H), 7.30 (dd, 1H), 7.07 (t, 1H), 6.79 (s, 1H), 6.01 (q, 1H), 4.87 (s, 2H), 3.75 (m, 1H), 3.25 (m, 1H), 2.68 (m, 2H), 2.59 (m, 2H), 2.40 (m, 1H), 2.05 (m, 1H), 1.82-1.68 (m, 17H), 1.56 (m, 1H).	562 [M+1]
I-436		1-(3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-1,1-dimethyl-prop-2-ynyl)-3-(2-morpholin-4-yl-ethyl)-urea	KI 1.11	11	(300MHZ, CDCl3) δ 7.72 (s, 1H), 7.31 (dd, 1H), 7.08 (t, 1H), 6.75 (s, 1H), 6.01 (q, 1H), 5.63 (bm, 1H), 5.00 (s, 2H), 4.66 (bs, 1H), 3.56 (m, 4H), 3.32 (m, 2H), 2.45 (m, 2H), 2.35 (m, 4H), 1.81 (d, 3H), 1.64 (s, 6H).	638 [M+1]
I-437		1-(3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-1,1-dimethyl-prop-2-ynyl)-3-(2-pyrrolidin-1-yl-ethyl)-urea	KI 0.61	11	(300MHZ, CDCl3) δ 7.72 (s, 1H), 7.31 (dd, 1H), 7.08 (t, 1H), 6.77 (s, 1H), 6.01 (q, 1H), 5.68 (bm, 1H), 5.14 (bs, 1H), 5.01 (s, 2H), 3.30 (m, 2H), 2.68 (m, 2H), 2.50 (m, 4H), 1.81 (d, 3H), 1.68 (m, 4H), 1.63 (s, 6H).	622 [M+1]
I-438		4-Pyrrolidin-1-yl-piperidine-1-carboxylic acid (3-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-1,1-dimethyl-prop-2-ynyl)-amide	KI 0.72	11	(300MHZ, CDCl3) δ 7.72 (s, 1H), 7.31 (dd, 1H), 7.07 (t, 1H), 6.78 (s, 1H), 6.01 (q, 1H), 5.65 (bm, 1H), 4.96 (s, 2H), 4.68 (bs, 1H), 3.56 (m, 2H), 2.62 (m, 2H), 2.56 (m, 4H), 2.28 (m, 1H), 1.92 (m, 2H), 1.81 (d, 5H), 1.80 (m, 4H), 1.70 (s, 6H), 1.50 (m, 2H).	562 [M+1]
I-439		3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-propynoic acid cyclohexylamide	KI 0.46	11	(300MHZ, CDCl3) δ 7.85 (d, 1H), 7.31 (dd, 1H), 7.09 (t, 1H), 6.78 (d, 1H), 6.00 (q, 1H), 5.69 (bd, 1H), 5.14 (s, 2H), 4.12 (m, 1H), 1.81 (d, 3H), 1.20 (d, 6H).	410 [M+1]
I-440		3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-propynoic acid isopropylamide	KI 0.43	11	(300MHZ, CDCl3) δ 7.86 (s, 1H), 7.31 (dd, 1H), 7.09 (t, 1H), 6.79 (s, 1H), 6.00 (q, 1H), 5.72 (bd, 1H), 5.14 (s, 2H), 3.82 (m, 1H), 1.85 (m, 2H), 1.80 (d, 3H), 1.72 (m, 2H), 1.65 (m, 2H), 1.38 (m, 2H), 1.20 (m, 2H).	460 [M+1]
I-441		4-(3-Amino-3-methyl-but-1-ynyl)-2-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-phenylamine	KI 1.08	11	(300MHZ, CD3OD) δ 7.80 (d, 1H), 7.45 (dd, 1H), 7.25 (t, 1H), 6.66 (d, 1H), 6.06 (q, 1H), 1.84 (d, 3H), 1.66 (s, 6H).	382 [M+1]

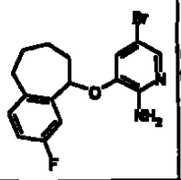
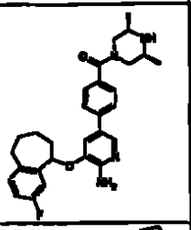
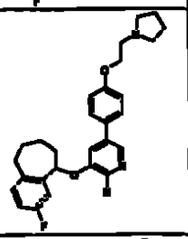
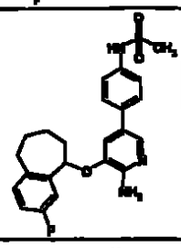
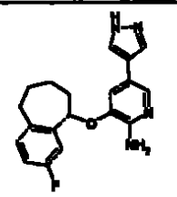
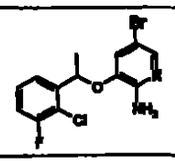
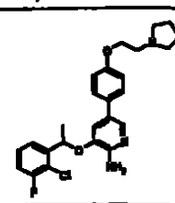
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-442		(4-[6-Amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone	16% at 1uM	13	(300MHZ, CDCl3) δ 7.90 (s, 1H), 7.51 (m, 1H), 7.40 (m, 5H), 7.10 (m, 1H), 6.90 (s, 1H), 5.80 (q, 1H), 4.94 (s, 2H), 3.58 (m, 4H), 2.53 (m, 4H), 2.32 (s, 3H), 1.84 (d, 3H).	503 [M+1]
I-443		(4-[6-Amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1yl)-methanone	13% at 1uM	13	(300MHZ, CDCl3) δ 7.89 (s, 1H), 7.54 (m, 1H), 7.32 (d, 5H), 7.17 (m, 1H), 6.90 (d, 1H), 5.79 (q, 1H), 4.93 (s, 2H), 4.60 (m, 1H), 3.80 (m, 1H), 2.95 (m, 2H), 2.54 (m, 4H), 2.34 (m, 1H), 1.85 (m, 2H), 1.81 (m, 4H),1.73 (d, 3H), 1.55 (m, 2H).	557 [M+1]
I-444		(4-[6-Amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone	10% at 1uM	13	(300MHZ, CDCl3) δ 7.9 (d, 1H), 7.50 (m, 1H), 7.36 (m, 5H), 7.11 (m, 1H), 6.90 (s, 1H), 5.81 (q, 1H), 4.93 (s, 2H), 4.62 (m, 1H), 3.66 (m, 1H), 2.85 (m, 2H), 2.65 (m, 1H), 2.40 (m, 1H), 1.73 (d, 3H), 1.10 (m, 7H).	517 [M+1]
I-445		(4-[6-Amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	15% at 1uM	13	(300MHZ, CDCl3) δ 7.90 (s, 1H), 7.73 (m, 1H), 7.53 (m, 3H), 7.34 (d, 2H), 7.13 (m, 1H), 6.90 (s, 1H), 5.80 (q, 1H), 4.93 (s, 2H), 4.45 (m, 1H), 3.50 (m, 2H), 2.70 (m, 4H), 1.73 (d, 3H), 1.20-2.0 (m, 10H).	557 [M+1]
I-446		(4-[6-Amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	12% at 1uM	13	(300MHZ, CDCl3) δ 7.90 (s, 1H), 7.73 (m, 1H), 7.53 (m, 3H), 7.34 (d, 2H), 7.13 (m, 1H), 6.90 (s, 1H), 5.80 (q, 1H), 4.93 (s, 2H), 4.45 (m, 1H), 3.50 (m, 2H), 2.70 (m, 4H), 1.73 (d, 3H), 1.20-2.0 (m, 10H).	557 [M+1]
I-449		4-[6-Amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-N-(1-methyl-piperidin-4-yl)-benzamide	12% at 1uM	13	(300MHZ, CDCl3) δ 7.90 (d, 1H), 7.78 (d, 2H), 7.72 (m, 1H), 7.52 (m, 1H), 7.46 (d, 2H), 7.10 (m, 1H), 6.89 (d,1H), 6.00 (bd, 1H), 5.80 (q, 1H), 4.93 (s, 2H), 4.02 (m, 1H), 2.85 (m, 2H), 2.31 (s, 3H), 2.16 (m, 2H), 2.05 (m, 2H), 1.73 (d, 3H), 1.62 (m, 2H).	517 [M+1]

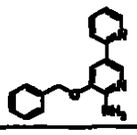
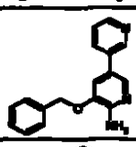
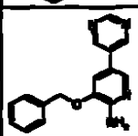
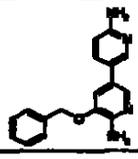
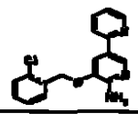
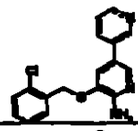
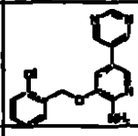
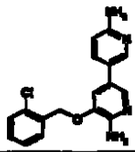
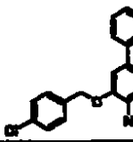
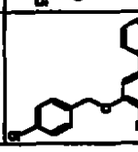
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-450		4-[6-Amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide	7% at 1uM	13	(300MHZ, CDCl3) δ 7.90 (d, 1H), 7.79 (d, 2H), 7.55 (m, 2H), 7.48 (d, 2H), 7.13 (m, 1H), 7.08 (bs, 1H), 6.90 (s, 1H), 6.80 (q, 1H), 4.94 (s, 2H), 3.58 (m, 2H), 2.78 (m, 2H), 2.62 (m, 4H), 1.81 (m, 4H), 1.72 (d, 3H).	517 [M+1]
I-451		4-[6-Amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide	12% at 1uM	13	(300MHZ, CDCl3) δ 7.91 (d, 1H), 7.78 (d, 2H), 7.51 (m, 2H), 7.39 (d, 2H), 7.10 (m, 1H), 6.91 (d, 1H), 6.78 (bs, 1H), 5.82 (q, 1H), 4.97 (s, 2H), 3.72 (m, 4H), 3.57 (m, 2H), 2.62 (m, 2H), 2.52 (m, 4H), 1.73 (d, 3H).	533 [M+1]
I-452		4-[6-Amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide	3% at 1uM	13	(300MHZ, CDCl3) δ 8.61 (s, 1H), 7.92 (s, 1H), 7.78 (d, 2H), 7.63 (m, 1H), 7.48 (d, 2H), 7.13 (m, 1H), 6.90 (s, 1H), 5.80 (q, 1H), 4.90 (s, 2H), 3.60 (m, 2H), 2.78 (m, 2H), 2.66 (m, 4H), 1.85 (m, 6H), 1.73 (d, 3H).	531 [M+1]
I-453		4-[6-Amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-N-(3-morpholin-4-yl-propyl)-benzamide	10% at 1uM	13	(300MHZ, CDCl3) δ 7.93 (s, 1H), 7.80 (d, 2H), 7.63 (m, 3H), 7.38 (d, 2H), 7.10 (m, 1H), 6.81 (d, 1H), 5.82 (q, 1H), 4.95 (s, 2H), 3.70 (m, 4H), 3.57 (m, 2H), 2.54 (m, 6H), 1.81 (m, 2H), 1.73 (d, 3H).	547 [M+1]
I-454		6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-nicotinonitrile	7% at 1uM	Example I-454	(400 MHz, DMSO-d6) δ 7.93 (s, 1H), 7.56 (m, 1H), 7.48 (t, 1H), 6.88 (br, 2H), 6.76 (s, 1H), 6.02 (q, 1H), 1.77(d, 3H).	326 [M-1]
I-455		6-Amino-5-[1-(2,6-dichloro-3-cyano-phenyl)-ethoxy]-nicotinonitrile	6% at 1uM	Example I-455	(400 MHz, DMSO-d6) δ 8.00 (s, 1H), 7.81 (d, 1H), 7.07 (t, 2H), 5.78 (d, 1H), 1.74(d, 3H).	332 [M-1]
I-456		5-Aminomethyl-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine	0% at 1 uM	Example I-456	(400 MHz, DMSO-d6) δ 7.53 (m, 1H), 7.43 (m, 2H), 6.78 (s, 1H), 6.68 (q, 1H), 5.47 (br, 2H), 1.74(d, 3H)	331 [M+1]
I-457		(R)-2-Pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-ylmethyl)-amide	1% at 1 uM	Example I-457	(400 MHz, DMSO-d6) δ 9.58(s,1H), 7.93(s,1H), 7.85(m,1H), 7.40(s,1H), 6.59 (dd,1H), 6.80 (d,1H), 6.08(q,1H), 4.19(dd,1H), 4.10(dd,1H), 3.94(dd,1H), 3.85(dd,1H), 3.21(m,2H), 3.15(m,2H), 3.01(m,2H), 1.98(m,2H), 1.90(m,2H), 1.84(m,2H), 1.78(d,3H), 1.72(br,1H).	511 [M+1]

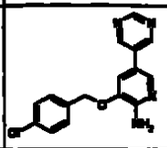
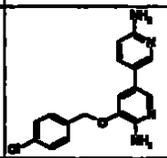
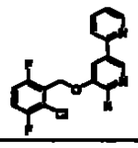
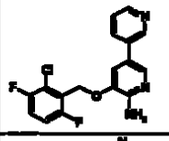
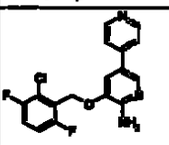
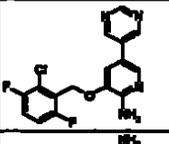
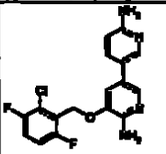
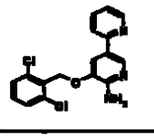
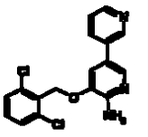
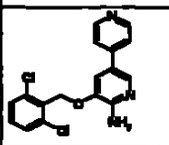
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-458		N-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-ylmethyl]-methanesulfonamide	0% at 1 uM	as in Example 13	(400 MHz, DMSO-d6) δ7.51 (m, 1H), 7.43 (t, 2H), 7.28(m, 1H), 6.70(s, 1H), 5.96(q, 1H), 5.68(s, 2H), 3.84(d, 2H), 2.68(s, 3H), 1.78(d, 3H)	409 [M+1]
I-459		N-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-ylmethyl]-acetamide	2% at 1 uM	as in Example 14 I	(400 MHz, CDCl3): d 7.49 (s, 1H), 7.29 (m, 1H), 7.08 (t, 1H), 6.71 (s, 1H), 6.03 (q, 1H), 5.49 (bs, 1H), 4.62 (bs, 2H), 4.29 (dd, 1H), 4.12 (dd, 1H), 1.99 (s, 3H), 1.83 (d, J 6.0 Hz, 3H).	372 [M+1]
I-460		N-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-ylmethyl]-4-methyl-benzenesulfonamide	9% at 1 uM	as in Example 13	(400 MHz, CDCl3): d 7.68 (d, 2H), 7.29 (m, 4H), 7.08 (t, 1H), 6.69 (s, 1H), 5.98 (q, 1H), 4.84 (bs, 2H), 4.51 (m, 1H), 3.88 (dt, 2H), 2.43 (s, 3H), 1.83 (d, J 6.0 Hz, 3H).	488 [M+1]
I-461		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-vinyl-pyridin-2-ylamine	Ki 0.68	3	(400 MHz, CDCl3): d 7.56 (s, 1H), 7.29 (m, 1H), 7.08 (t, 1H), 6.91 (s, 1H), 6.19 (dd, 1H), 6.07 (q, 1H), 5.40 (d, J 16Hz, 1H), 5.02 (d, J 12 Hz, 1H), 4.85 (bs, 2H), 1.85 (d, J 6.0 Hz, 3H).	327 [M+1]
I-462		(S)-1-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-ethane-1,2-diol	2% at 1 uM	Example I-462	(400 MHz, CDCl3): d 7.55 (s, 1H), 7.29 (m, 1H), 7.08 (t, 1H), 6.82 (s, 1H), 6.09 (q, 1H), 4.82 (bs, 2H), 4.63 (m, 1H), 3.54 (m, 4H), 1.83 (d, J 6.0 Hz, 3H).	382 [M+1]
I-463		(R)-1-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-ethane-1,2-diol	2% at 1 uM	as in Example I-462	(400 MHz, CDCl3): d 7.56 (s, 1H), 7.29 (m, 1H), 7.08 (t, 1H), 6.82 (s, 1H), 6.06 (q, 1H), 4.82 (bs, 2H), 4.63 (m, 1H), 3.54 (m, 4H), 1.83 (d, J 6.0 Hz, 3H).	382 [M+1]
I-464		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(1H-pyrazol-4-yl)-pyridin-2-ylamine	Ki 0.10	3	(400 MHz, CDCl3): d 7.85 (s, 2H), 7.52 (s, 1H), 7.37 (m, 1H), 7.13 (m, 1H), 7.04 (s, 1H), 6.17 (q, J 6.0 Hz, 1H), 1.93 (d, J 6.0 Hz, 3H)	367 [M+1]
I-465		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-[1-(2-pyrrolidin-1-yl-ethyl)-1H-pyrazol-4-yl]-pyridin-2-ylamine	Ki 0.34	14	(400 MHz, CDCl3): d 7.71 (s, 1H), 7.55 (s, 2H), 7.37 (m, 1H), 7.08 (m, 1H), 6.87 (s, 1H), 6.09 (m, 1H), 4.29 (t, J 6.0 Hz, 2H), 2.96 (t, J 6.0 Hz, 2H), 2.68 (m, 4H), 1.87 (d, J 6.0 Hz, 3H), 1.28 (m, 4H)	465 [M+1]
I-466		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-[1-(2-diisopropylamino-ethyl)-1H-pyrazol-4-yl]-pyridin-2-ylamine	Ki 0.47	14	(400 MHz, CDCl3): d 7.76 (s, 1H), 7.54 (s, 1H), 7.46 (s, 1H), 7.28 (m, 1H), 7.04 (m, 1H), 6.85 (m, 1H), 6.08 (m, 1H), 4.05 (t, J 6.0 Hz, 2H), 2.83 (t, 2H), 1.88 (d, J 4.0 Hz, 3H), 0.99 (d, J 6.0 Hz, 12H).	496 [M+1]

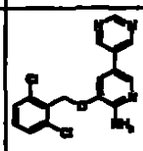
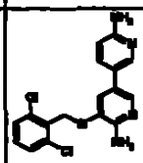
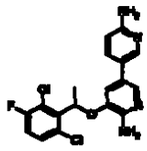
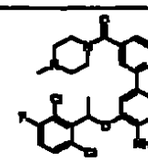
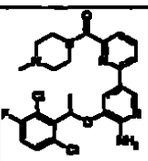
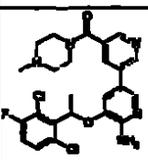
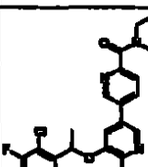
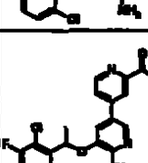
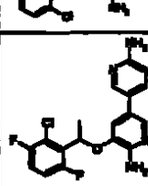
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-467		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-[1-(2-morpholin-4-yl-ethyl)-1H-pyrazol-4-yl]-pyridin-2-ylamine	KI 0.053	14	(400 MHz, CDCl3): d 7.72 (s, 1H), 7.60 (s, 1H), 7.50 (s, 1H), 7.38 (m, 1H), 7.13 (m, 1H), 7.05 (s, 1H), 6.19 (m, 1H), 4.81 (m, 2H), 3.89 (m, 4H), 3.63 (m, 2H), 3.02 (m, 4H), 1.93 (d, J 6.0 Hz, 3H).	481 [M+1]
I-468		5-Bromo-3-(3-fluoro-2-methoxy-benzyloxy)-pyridin-2-ylamine	8% at 1uM	16	(400 MHz, DMSO-d6) δ 7.87 (s, 1H), 7.43 (d, 1H), 7.40(d, 1H), 7.33(t, 1H), 7.20(m, 1H), 6.00(s, 2H), 5.19 (s, 2H), 3.99(s, 3H)	326 [M+1]
I-469		5-Bromo-3-[1-(3-fluoro-2-methoxy-phenyl)-ethoxy]-pyridin-2-ylamine	7% at 1uM	15	(400 MHz, DMSO-d6) δ 7.51 (s, 1H), 7.25 (d, 1H), 7.16(m, 1H), 7.06(m, 1H), 6.94(s, 1H), 6.02(s, 2H), 5.72 (q, 1H), 3.93(s, 3H), 1.57(d, 3H)	342 [M+1]
I-470		(1-[5-Amino-5-(3-fluoro-2-methoxy-benzyloxy)-pyridin-3-yl]-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone	3% at 1uM	3	(400 MHz, DMSO-d6) δ 9.24(s, 1H), 8.61(d,1H), 7.96(d, 1H), 7.81(d, 2H), 7.57 (d, 1H), 7.43 (d, 2H), 7.32(t, 1H), 7.18(m, 1H), 6.34(s, 2H), 3.91(s, 3H), 3.39 (m, 2H), 2.49(m, 4H), 1.21(m, 6H).	485 [M+1]
I-471		(4-[5-Amino-5-[1-(3-fluoro-2-methoxy-phenyl)-ethoxy]-pyridin-3-yl)-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone	1% at 1μM	3	(400 MHz, DMSO-d6) δ 9.25(d, 1H), 8.64(d,1H), 7.88(s, 1H), 7.81(d, 2H), 7.63 (d, 2H), 7.46 (s, 1H), 7.25(d, 1H), 7.21(t, 1H), 7.13(m, 1H), 6.03(m, 1H), 3.93(s, 3H), 3.35(m, 2H), 2.49 (m, 4H), 1.67(d, 3H), 1.20(m, 6H)	479 [M+1]
I-472		5-Bromo-3-(3-fluoro-2-isopropoxy-benzyloxy)-pyridin-2-ylamine	KI 12.1	15	(400 MHz, DMSO-d6) δ 7.89 (s, 1H), 7.36 (d, 1H), 7.31(d, 1H), 7.25(t, 1H), 7.12(m, 1H), 5.90(s, 2H), 5.10(s, 2H), 4.43 (m, 1H),1.29(d, 6H)	356
I-473		(4-[5-Amino-5-(3-fluoro-2-isopropoxy-benzyloxy)-pyridin-3-yl]-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone	KI 12.7	3	(400 MHz, DMSO-d6) δ 9.45(d, 1H), 8.79(q,1H), 7.99(s, 1H), 7.88(s, 1H), 7.80 (d, 2H), 7.58 (d, 2H), 7.41(d, 1H), 7.32(t, 1H), 7.17(m, 1H), 5.37(s, 2H), 4.45(m, 1H), 3.40(m, 2H), 2.49 (m, 4H), 1.28(d, 6H), 1.20 (m, 6H)	493

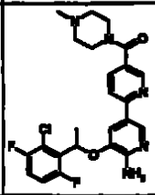
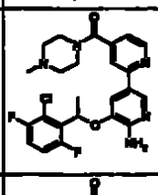
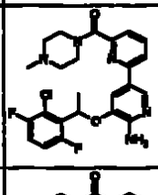
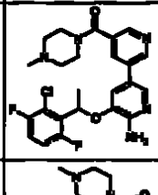
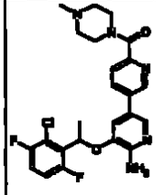
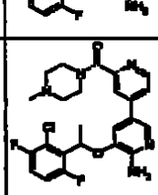
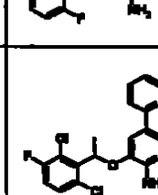
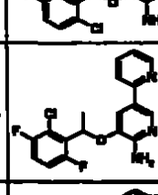
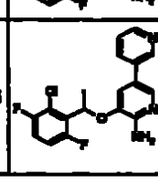
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-474		5-(4-Amino-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine		3	(400 MHz, DMSO-d6) δ 7.68(d, 1H), 7.55(q, 1H), 7.43 (t, 1H), 7.02 (d, 2H), 6.81(s, 1H), 6.66(d, 2H), 6.06(q, 1H), 5.80(s, 2H), 5.08(s, 2H), 1.78(d, 3H)	393
I-475		(4-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenoxy)-acetic acid methyl ester	Ki 0.20	as in Example 65	(400 MHz, CDCl3): d 7.82 (s, 1H), 7.30 (m, 3H), 7.08 (m, 1H), 6.95 (m, 3H), 6.12 (q, 1H), 4.80 (m, 2H), 4.68 (s, 2H), 3.82 (s, 3H), 1.88 (d, J 8.0 Hz, 3H).	457
I-476		(4-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenoxy)-acetic acid	Ki 0.20	as in Example 65	(400 MHz, CDCl3): d 7.70 (s, 1H), 7.50 (m, 2H), 7.45 (m, 2H), 7.20 (m, 2H), 6.85 (m, 2H), 6.05 (q, 1H), 5.72 (s, 2H), 4.49 (s, 2H), 3.82 (s, 3H), 1.75 (d, J 8.0 Hz, 3H).	453
I-477		2-(4-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenoxy)-1-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-ethanone	Ki 0.027	4	(400 MHz, CDCl3): d 7.48 (s, 1H), 7.36 (m, 1H), 7.20 (m, 2H), 7.12 (m, 2H), 7.01 (m, 2H), 6.20 (q, 1H), 4.73 (m, 3H), 4.10 (m, 1H), 3.36 (m, 1H), 3.13 (m, 2H), 2.84 (m, 1H), 1.94 (d, J 8.0 Hz, 3H), 1.34 (m, 6H).	548
I-478		2-(4-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenoxy)-1-((R)-3-hydroxy-pyrrolidin-1-yl)-ethanone	Ki 0.041	4	(400 MHz, CDCl3): d 7.48 (s, 1H), 7.36 (m, 1H), 7.21 (d, 2H), 7.19 (m, 2H), 7.10 (m, 2H), 7.01 (m, 2H), 6.20 (q, 1H), 4.65 (m, 2H), 4.55 (m, 1H), 3.69 (m, 3H), 3.48 (m, 1H), 2.10 (m, 3H), 1.92 (m, 5H).	521
I-479		4-[2-(4-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenoxy)-acetyl]-piperazine-1-carboxylic acid tert-butyl ester	Ki 0.18	4	(400 MHz, CDCl3): d 7.50 (s, 1H), 7.38 (m, 1H), 7.22 (d, 2H), 7.19 (m, 2H), 7.15 (m, 2H), 7.00 (m, 2H), 6.20 (q, 1H), 4.75 (s, 2H), 3.57 (m, 4H), 3.48 (m, 4H), 1.93 (d, J 8.0 Hz, 3H), 1.47 (s, 9H).	620
I-480		2-(4-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenoxy)-1-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-ethanone		4	(400 MHz, CDCl3): d 7.48 (s, 1H), 7.36 (m, 1H), 7.20 (d, 2H), 7.15 (m, 2H), 7.00 (d, 2H), 6.20 (q, 1H), 4.68 (s, 2H), 4.48 (m, 1H), 4.04 (m, 1H), 3.93 (m, 1H), 3.80 (m, 1H), 3.62 (m, 1H), 3.50 (m, 1H), 3.12 (m, 1H), 3.09 (m, 1H), 2.83 (m, 1H), 1.93 (d, J 8.0 Hz, 3H), 2.16-1.68 (m, 10H).	588

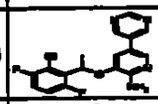
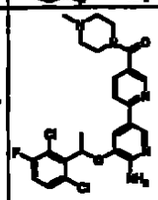
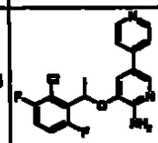
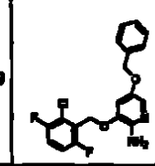
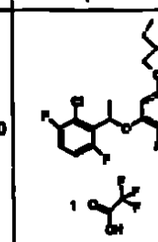
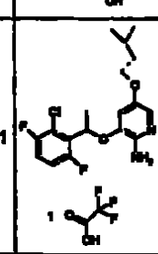
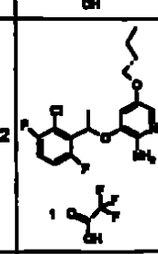
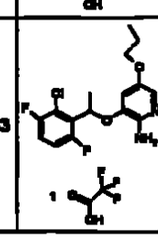
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-481		6-Bromo-3-(3-fluoro-6,7,8,9-tetrahydro-5*H*-benzocycloheptan-5-yloxy)-pyridin-2-ylamine		15	(400 MHz, DMSO-d6) δ 7.57 (d, 1H), 7.16 (m, 3H), 6.98(d, 1H), 6.07(d, 2H), 5.63(d, 1H), 2.10(m, 2H), 2.16(m, 2H), 1.88 (m, 1H),1.77(m, 2H), 1.34(m,1H).	352
I-482		(4-[6-Amino-5-(3-fluoro-6,7,8,9-tetrahydro-5H-benzocycloheptan-5-yloxy)-pyridin-3-yl]-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone		3		483
I-483		3-(3-Fluoro-6,7,8,9-tetrahydro-5H-benzocycloheptan-5-yloxy)-6-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-pyridin-2-ylamine		3		482
I-484		N-[4-[6-Amino-5-(3-fluoro-6,7,8,9-tetrahydro-5H-benzocycloheptan-5-yloxy)-pyridin-3-yl]-phenyl]-methanesulfonamide		3		442
I-485		3-(3-Fluoro-6,7,8,9-tetrahydro-5H-benzocycloheptan-5-yloxy)-5-(1H-pyrazol-4-yl)-pyridin-2-ylamine		3		337 [M-1]
I-486		6-Bromo-3-[1-(2-chloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine	0% at 1 uM	15	(400 MHz, CDCl3): d 7.68 (s, 1H), 7.24 (m, 3H), 6.69 (s, 1H), 5.84 (q, 1H), 4.78 (bs, 2H), 1.88 (d, J 8.0 Hz, 3H).	347
I-487		3-[1-(2-Chloro-3-fluoro-phenyl)-ethoxy]-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-pyridin-2-ylamine	Ki 3.30	3	(400 MHz, CDCl3): d 7.80 (s, 1H), 7.30 (m, 2H), 7.20 (m, 3H), 7.00 (s, 1H), 6.95 (m, 2H), 5.90 (q, 1H), 4.36 (m, 2H), 3.86 (m, 2H), 3.55 (m, 2H), 2.95 (m, 2H), 2.10 (m, 4H), 1.82 (d, J 8.0 Hz, 3H).	456

No.	Structure	Name	Met IC$_{50}$ (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-488		5'-Benzyloxy-[2,3']bipyridinyl-6'-ylamine	>20	16	(CDCl3) d 5.16 (br s, 2H), 5.19 (s, 2H), 7.17 (m, 1H), 7.34-7.48 (m, 5H), 7.84 (d, J = 8 Hz, 1H), 7.70 (td, J = 7.8, 1.9 Hz, 1H), 7.88 (d, J = 1.6 Hz, 1H), 8.22 (d, J = 2 Hz, 1H), 8.63 (d, J = 4 Hz, 1H).	278
I-489		6-Benzyloxy-[3,3']bipyridinyl-6-ylamine	>20	16	(CDCl3) d 5.17 (s, 2H), 5.27 (br s, 2H), 7.19 (d, J = 2 Hz, 1H), 7.33 (dd, J = 7.8, 4.8 Hz, 1H), 7.35-7.44 (m, 5H), 7.70 (dt, J = 2, 8 Hz, 1H), 7.85 (d, J = 2 Hz, 1H), 8.58 (dd, J = 1.8, 4.8 Hz, 1H), 8.71 (d, J = 2 Hz, 1H).	278
I-490		3-Benzyloxy-5-pyrimidin-5-yl-pyridin-2-ylamine	>20	16	(CDCl3) d 5.22 (s, 2H), 6.15 (br s, 2H), 7.21 (s, 1H), 7.43 (m, 5H), 7.77 (s, 1H), 8.81 (s, 2H), 9.20 (s, 1H).	279
I-491		5-Benzyloxy-[3,3']bipyridinyl-6,6'-diamine	>20	16	(CDCl3) d 4.40 (br s, 2H), 4.94 (br s, 2H), 5.13 (s, 2H), 6.58 (d, J = 8.4 Hz, 1H), 7.09 (d, J = 1.8 Hz, 1H), 7.35-7.44 (m, 5H), 7.59 (dd, J = 2.4, 8.4 Hz, 1 H), 7.77 (d, J = 1.8 Hz, 1H), 8.13 (d, J = 2 Hz, 1H).	293
I-492		5'-(2-Chloro-benzyloxy)-[2,3']bipyridinyl-6'-ylamine	8.24	16	(CDCl3) d 5.33 (s, 2H), 6.99 (bs, 2H), 7.22-7.26 (m, 1H), 7.29-7.37 (m, 2H), 7.42-7.51 (m, 2H), 7.63 (d, 1H), 7.72 (dt, 1H), 7.99 (d, 1H), 8.13 (d, 1H), 8.86 (dd, 1H).	312
I-493		5-(2-Chloro-benzyloxy)-[3,3']bipyridinyl-6-ylamine	4.6	16		312
I-494		3-(2-Chloro-benzyloxy)-5-pyrimidin-5-yl-pyridin-2-ylamine	12.3	16		315
I-495		5-(2-Chloro-benzyloxy)-[3,3']bipyridinyl-6,6'-diamine	4.31	16		317
I-496		5'-(4-Chloro-benzyloxy)-[2,3']bipyridinyl-6'-ylamine	14	16	(CDCl3) d 5.16 (s, 2H), 6.48 (bs, 2H), 7.19-7.22 (m, 1H), 7.38 (s, 4H), 7.83-7.85 (m, 1H), 7.73 (dt, 1H), 7.89 (d, 1H), 8.17 (d, 1H), 8.83 (d, 1H).	312
I-497		5-(4-Chloro-benzyloxy)-[3,3']bipyridinyl-6-ylamine	14.1	16		312

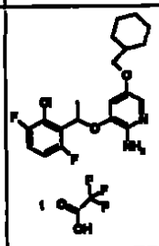
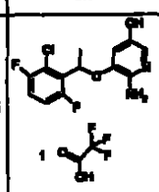
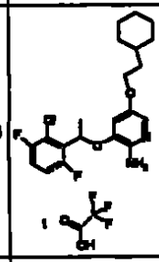
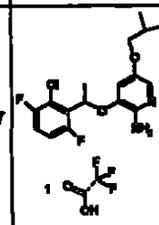
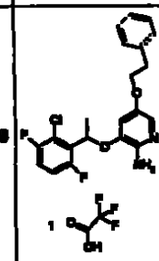
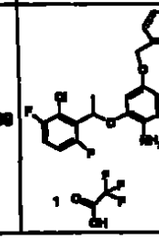
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-498		3-(4-Chloro-benzyloxy)-5-pyrimidin-5-yl-pyridin-2-ylamine	>20.0	16		313
I-499		6-(4-Chloro-benzyloxy)-[3,3']bipyridinyl-6,6'-diamine	>20.0	16		317
I-500		5'-(2-Chloro-3,6-difluoro-benzyloxy)-[2,3']bipyridinyl-6'-ylamine	1.8	16	(CDCl3) δ 5.39 (s, 2H), 6.19 (bs, 2H), 7.08 (dt, 1H), 7.21-7.28 (m, 2H), 7.85 (d, 1H), 7.77 (dt, 1H), 8.13 (d, 1H), 8.67 (dd, 1H)	349
I-501		6-(2-Chloro-3,6-difluoro-benzyloxy)-[3,3']bipyridinyl-6-ylamine	0.282	16		349
I-502		5-(2-Chloro-3,6-difluoro-benzyloxy)-[3,4']bipyridinyl-6-ylamine	0.211	16		349
I-503		3-(2-Chloro3,6-difluoro-benzyloxy)-5-pyrimidin-5-yl-pyridin-2-ylamine	2.16	16		349
I-504		5-(2-Chloro-3,6-difluoro-benzyloxy)-[3,3']bipyridinyl-6,6'-diamine	0.209	16		363
I-505		5'-(2,6-Dichloro-benzyloxy)-[2,3']bipyridinyl-6'-ylamine	2.84	16	(CDCl3) d 5.47 (s, 2H), 6.76 (bs, 2H), 7.21-7.25 (m, 1H), 7.27-7.32 (m, 1H), 7.37-7.41 (m, 2H), 7.98 (d, 1H), 7.75 (dt, 1H), 8.06 (d, 1H), 8.17 (d, 1H), 8.68 (dd, 1H).	348
I-506		6-(2,6-Dichloro-benzyloxy)-[3,3']bipyridinyl-6-ylamine	2.71	16		348
I-507		5-(2,6-Dichloro-benzyloxy)-[3,4']bipyridinyl-6-ylamine	1.3	16		348

No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-508		3-(2,6-Dichloro-benzyloxy)-5-pyrimidin-5-yl-pyridin-2-ylamine	10.3	16		347
I-509		5-(2,6-Dichloro-benzyloxy)-[3,3']bipyridinyl-6,6'-diamine	0.678	16		361
I-510		5-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6,6'-diamine	0.0167	16	(CDCl3) d 1.87 (d, J = 6.6 Hz, 3H), 4.60 (br s, 2H), 4.66 (br s, 2H), 6.11 (q, J = 6.6 Hz, 1H), 6.68 (d, J = 8.4 Hz, 1H), 6.91 (s, 1H), 7.08 (t, J = 8.5 Hz, 1H), 7.31 (dd, J = 4.9, 8.7 Hz, 1H), 7.48 (dd, J = 1.8, 8.4 Hz, 1H), 7.78 (s, 1H), 8.06 (s, 1H).	393
I-511		(6'-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-4-yl)-(4-methyl-piperazin-1-yl)-methanone	0.0742	16	(CDCl3) d 1.87 (d, J = 6.6 Hz, 3H), 2.37 (s, 3H), 2.39 (br s, 2H), 2.58 (br s, 2H), 3.43 (br s, 2H), 3.88 (br s, 2H), 6.13 (br s, 2H), 6.21 (q, J = 6.7 Hz, 1H), 7.04 (dd, J = 8.1, 8.7 Hz, 1H), 7.10 (dd, J = 1.2, 5.1 Hz, 1H), 7.29 (dd, J = 5.1, 9.3 Hz, 1H), 7.48 (s, 1H), 7.57 (d, J = 1.5 Hz, 1H), 8.24 (d, J = 1.5 Hz, 1H), 8.66 (dd, J = 0.6, 4.8 Hz, 1H).	504
I-512		(6'-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6-yl)-(4-methyl-piperazin-1-yl)-methanone	0.0629	16	(CDCl3) d 1.87 (d, J = 6.6 Hz, 3H), 2.36 (s, 3H), 2.48 (m, 2H), 2.56 (m, 2H), 3.66 (m, 2H), 3.89 (m, 2H), 5.09 (br s, 2H), 6.17 (q, J = 6.6 Hz, 1H), 7.05 (dd, J = 8.1, 8.8 Hz, 1H), 7.31 (dd, J = 5.0, 8.9 Hz, 1H), 7.48 (dd, J = 0.8, 7.7 Hz, 1H), 7.61 (d, J = 1.8 Hz, 1H), 7.86 (dd, J = 0.8, 8.0 Hz, 1H), 7.76 (t, J = 7.8 Hz, 1H), 8.27 (d, J = 1.2 Hz, 1H).	504
I-513		(6'-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6-yl)-(4-methyl-piperazin-1-yl)-methanone	0.034	16	(CDCl3) d 1.88 (d, J = 6.6 Hz, 3H), 2.39 (s, 3H), 2.43 (m, 2H), 2.56 (m, 2H), 3.52 (m, 2H), 3.87 (m, 2H), 5.05 (br s, 2H), 6.12 (q, J = 6.7 Hz, 1H), 6.97 (d, J = 1.5 Hz, 1H), 7.08 (dd, J = 8.1, 8.7 Hz, 1H), 7.23 (dd, J = 5.0, 8.9 Hz, 1H), 7.72 (t, J = 2.1 Hz, 1H), 7.86 (d, J = 2.1 Hz, 1H), 8.54 (d, J = 1.8 Hz, 1H), 8.66 (d, J = 2.4 Hz, 1H).	504
I-514		(6'-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6-yl)-(4-methyl-piperazin-1-yl)-methanone	0.0213	16	(CDCl3) d 1.88 (d, J = 6.9 Hz, 3H), 2.39 (s, 3H), 2.62 (br s, 2H), 2.81 (br s, 2H), 3.74 (br s, 2H), 3.89 (br s, 2H), 5.02 (br s, 2H), 6.12 (q, J = 6.7 Hz, 1H), 6.97 (d, J = 1.2 Hz, 1H), 7.08 (t, J = 8.4 Hz, 1H), 7.33 (dd, J = 4.8, 8.7 Hz, 1H), 7.89 (d, J = 9 Hz, 1H), 7.76 (dd, J = 1.8, 8.4 Hz, 1H), 7.89 (d, J = 1.5 Hz, 1H), 8.59 (d, J = 1.5 Hz, 1H).	504
I-515		(6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[2,4']bipyridinyl-2'-yl)-(4-methyl-piperazin-1-yl)-methanone	0.0367	16	(CDCl3) d 1.88 (d, J = 6.9 Hz, 3H), 2.39 (s, 3H), 2.61 (m, 2H), 2.81 (m, 2H), 3.67 (m, 2H), 3.90 (m, 2H), 5.06 (br s, 2H), 6.14 (q, J = 6.7 Hz, 1H), 7.05 (s, 1H), 7.09 (dd, J = 7.8, 9 Hz, 1H), 7.32 (d, J = 5.1 Hz, 1H), 7.34 (dd, J = 5.0, 7.7 Hz, 1H), 7.69 (d, J = 1.2 Hz, 1H), 8.00 (d, J = 1.8 Hz, 1H), 8.53 (d, J = 5.1 Hz, 1H).	504
I-516		5-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6,6'-diamine	0.0303	16	(CDCl3) d 1.83 (d, J = 6.6 Hz, 3H), 4.55 (br s, 2H), 4.67 (br s, 2H), 6.06 (q, J = 6.5 Hz, 1H), 6.66 (d, J = 8.4 Hz, 1H), 6.93-7.12 (m, 3H), 7.48 (dd, J = 1.8, 8.4 Hz, 1H), 7.76 (s, 1H), 8.08 (s, 1H).	377

No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS *m/z* (M+1)
I-517		(5'-Amino-5'-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-6-yl)-(4-methyl-piperazin-1-yl)-methanone	0.131	16	(CDCl3) d 1.84 (d, J = 6.6 Hz, 3H), 2.39 (s, 3H), 2.53 (br s, 4H), 3.63 (br s, 2H), 3.82 (br s, 2H), 5.09 (br s, 2H), 6.08 (q, J = 6.5 Hz, 1H), 6.93-7.10 (m, 2H), 7.60 (d, J = 7.8 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1H), 7.76 (dd, J = 2.1, 8.4 Hz, 1H), 8.28 (d, J = 1.5 Hz, 1H), 8.66 (d, J = 1.5 Hz, 1H).	488
I-518		(5'-Amino-5'-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-4-yl)-(4-methyl-piperazin-1-yl)-methanone	0.209	16	(CDCl3) d 1.84 (d, J = 6.6 Hz, 3H), 2.40 (s, 3H), 2.46 (br s, 2H), 2.61 (br s, 2H), 3.48 (br s, 2H), 3.69 (br s, 2H), 5.13 (br s, 2H), 6.06 (q, J = 6.6 Hz, 1H), 6.93-7.10 (m, 2H), 7.12 (dd, J = 1.2, 5.1 Hz, 1H), 7.52 (s, 1H), 7.68 (d, J = 1.2 Hz, 1H), 8.24 (d, J = 1.8 Hz, 1H), 8.67 (d, J = 4.8 Hz, 1H).	488
I-519		(5'-Amino-5'-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-5-yl)-(4-methyl-piperazin-1-yl)-methanone	0.466	16	(CDCl3) d 1.84 (d, J = 6.6 Hz, 3H), 2.38 (s, 3H), 2.49 (m, 2H), 2.60 (m, 2H), 3.70 (m, 2H), 3.81 (m, 2H), 5.01 (br s, 2H), 6.02 (q, J = 6.6 Hz, 1H), 6.93-7.12 (m, 2H), 7.49 (dd, J = 0.8, 7.7 Hz, 1H), 7.58 (dd, J = 0.9, 8.1 Hz, 1H), 7.62 (d, J = 1.8 Hz, 1H), 7.78 (t, J = 7.8 Hz, 1H), 8.29 (d, J = 1.8 Hz, 1H).	488
I-520		(5'-Amino-5'-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-5-yl)-(4-methyl-piperazin-1-yl)-methanone	0.134	16	(CDCl3) d 1.85 (d, J = 6.6 Hz, 3H), 2.44 (s, 3H), 2.57 (m, 4H), 3.69 (m, 2H), 3.91 (m, 2H), 5.02 (br s, 2H), 5.97 (q, J = 6.4 Hz, 1H), 6.96-7.14 (m, 3H), 7.74 (s, 1H), 7.97 (br s, 1H), 8.57 (br s, 1H), 8.71 (br s, 1H).	488
I-521		(5'-Amino-5'-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6-yl)-(4-methyl-piperazin-1-yl)-methanone	0.0716	16	(CDCl3) d 1.86 (d, J = 6.6 Hz, 3H), 2.45 (s, 3H), 2.62 (br s, 2H), 2.69 (br s, 2H), 3.82 (br s, 2H), 3.95 (br s, 2H), 4.97 (br s, 2H), 5.98 (q, J = 6.6 Hz, 1H), 6.96-7.14 (m, 3H), 7.71 (d, J = 8.1 Hz, 1H), 7.79 (dd, J = 2.3, 8.3 Hz, 1H), 7.90 (d, J = 2.1 Hz, 1H), 8.62 (d, J = 1.5 Hz, 1H).	488
I-522		(5-Amino-5-[1-(3-chloro-3,6-difluoro-phenyl)-ethoxy]-[3,4']bipyridinyl-2'-yl)-(4-methyl-piperazin-1-yl)-methanone	0.0626	16	(CDCl3) d 1.86 (d, J = 6.6 Hz, 3H), 2.45 (s, 3H), 2.62 (br s, 2H), 2.70 (br s, 2H), 3.77 (br s, 2H), 3.96 (br s, 2H), 5.03 (br s, 2H), 5.99 (q, J = 6.7 Hz, 1H), 6.96-7.14 (m, 2H), 7.16 (d, J = 1.8 Hz, 1H), 7.36 (dd, J = 2.0, 8.3 Hz, 1H), 7.71 (d, J = 1.2 Hz, 1H), 8.01 (d, J = 1.8 Hz, 1H), 8.45 (d, J = 4.8 Hz, 1H).	488
I-523		5'-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-6'-ylamine	0.0577	16	(CDCl3) d 1.87 (d, J = 6.6 Hz, 3H), 5.20 (br s, 2H), 6.23 (q, J = 6.7 Hz, 1H), 7.04 (t, J = 8.4 Hz, 1H), 7.16 (dd, J = 4.8, 8.8 Hz, 1H), 7.29 (dd, J = 5.1, 8.3 Hz, 1H), 7.51 (d, J = 8.1 Hz, 1H), 7.69 (d, J = 1.2 Hz, 1H), 7.87 (td, J = 7.8, 1.8 Hz, 1H), 8.24 (d, J = 1.5 Hz, 1H), 8.60 (d, J = 3.9 Hz, 1H).	378
I-524		5'-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-6'-ylamine	0.612	16	(CDCl3) d 1.84 (d, J = 6.9 Hz, 3H), 5.14 (br s, 2H), 6.06 (q, J = 6.6 Hz, 1H),6.93-7.10 (m, 2H), 7.16 (dd, J = 5.1, 8.6 Hz, 1H), 7.54 (d, J = 8.1 Hz, 1H), 7.65-7.70 (m, 2H), 8.24 (s, 1H), 8.62 (d, J = 4.2 Hz, 1H)	382
I-525		5-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6-ylamine	0.0777	16	(CDCl3) d 1.87 (d, J = 6.6 Hz, 3H), 5.37 (br s, 2H), 6.00 (q, J = 6.5 Hz, 1H), 6.97-7.15 (m, 3H), 7.34 (dd, J = 4.7, 7.7 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1H), 7.82 (s, 1H), 8.38 (d, J = 3.9 Hz, 1H), 8.85 (s, 1H).	382

No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-626		3-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-5-pyrimidin-5-yl-pyridin-2-ylamine	0.582	16	(CDCl3) d 1.87 (d, J = 6.6 Hz, 3H), 5.16 (br s, 2H), 5.99 (q, J = 6.5 Hz, 1H), 6.95-7.14 (m, 3H), 7.85 (s, 1H), 8.77 (s, 2H), 9.14 (s, 1H).	363
I-627		(5'-Amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-5-yl)-(4-methyl-piperazin-1-yl)-methanone	0.0385	16	(CDCl3) d 1.87 (d, J = 6.6 Hz, 3H), 2.36 (s, 3H), 2.51 (bra, 4H), 3.82 (br s, 2H), 3.81 (br s, 2H), 5.13 (br s, 2H), 6.21 (q, J = 6.7 Hz, 1H), 7.04 (t, J = 8.4 Hz, 1H), 7.30 (dd, J = 4.5, 8.7 Hz, 1H), 7.76 (dd, J = 1.9, 8.2 Hz, 1H), 8.28 (s, 1H), 8.84 (s, 1H).	504
I-628		5-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-[3,4']bipyridinyl-6-ylamine	0.0859	16	(CDCl3) d 1.84 (d, J = 6 Hz, 3H), 5.13 (br s, 2H), 5.97 (q, J = 6.5 Hz, 1H), 6.95-7.10 (m, 2H), 7.12 (d, J = 1.5 Hz, 1H), 7.30 (d, J = 6 Hz, 2H), 7.95 (d, J = 2 Hz, 1H), 8.56 (d, J = 5.9 Hz, 2H).	362
I-629		6-Benzyloxy-3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-2-ylamine	2.66	17	(CDCl3) d 1.84 (d, 3H), 4.89 (s, 2H), 5.89 (q, 1H), 6.79 (d, 1H), 6.41 (d, 1H), 7.01 (dt, 1H), 7.11 7.17 (m, 1H), 7.28-7.40 (m, 5H).	391
I-630		3-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-5-(2-ethyl-butoxy)-pyridin-2-ylamine	4.08	17		385
I-631		3-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-5-(3-methyl-butoxy)-pyridin-2-ylamine	2.4	17		371
I-632		3-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-5-butoxy-pyridin-2-ylamine	1.94	17		357
I-633		3-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-5-propoxy-pyridin-2-ylamine	0.572	17		343

112

No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-634		3-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-5-cyclohexylmethoxy-pyridin-2-ylamine	6.97	17		397
I-635		6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-ol	0.64	17		301
I-636		3-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-5-(2-cyclohexyl-ethoxy)-pyridin-2-ylamine	7.5	17		411
I-637		3-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-5-isobutoxy-pyridin-2-ylamine	1.2	17		357
I-638		3-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-5-phenethyloxy-pyridin-2-ylamine	2.8	17		405
I-639		3-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-5-(pyridin-2-ylmethoxy)-pyridin-2-ylamine	3.2	17		392

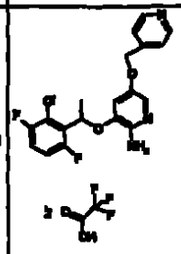
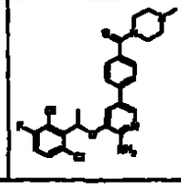
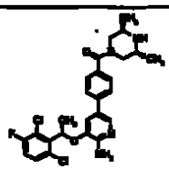
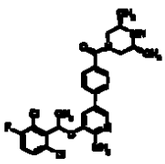
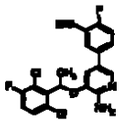
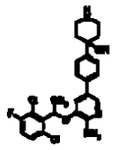
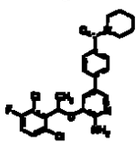
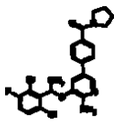
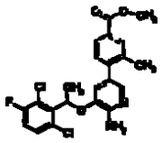
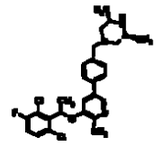
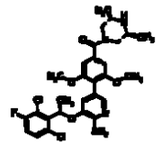
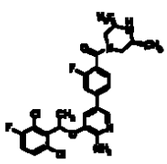
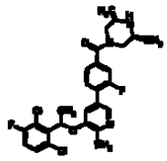
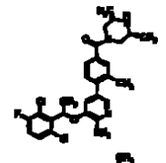
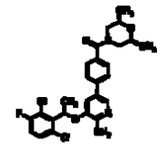
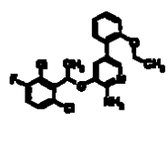
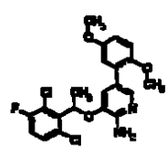
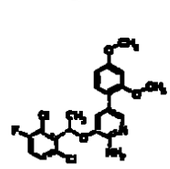
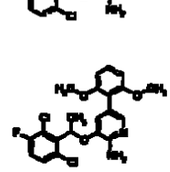
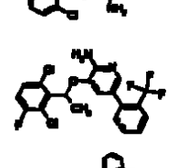
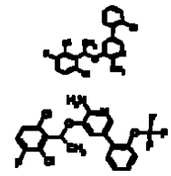
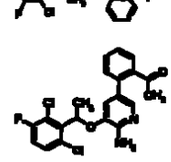
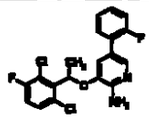
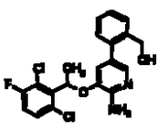
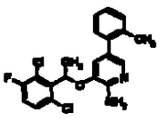
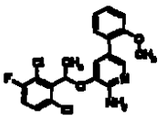
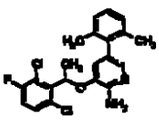
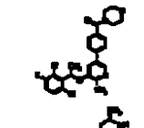
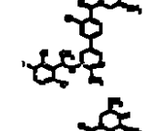
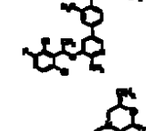
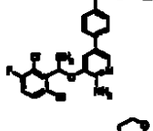
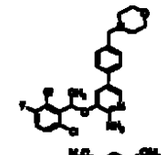
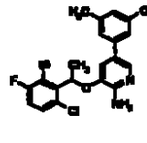
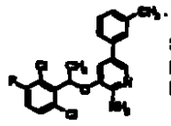
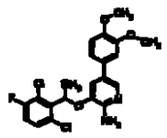
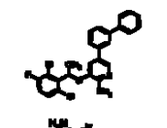
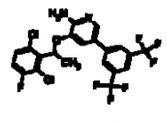
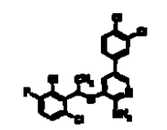
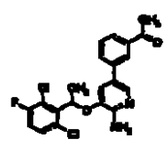
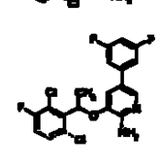
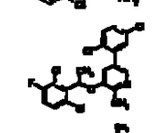
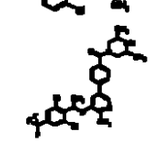
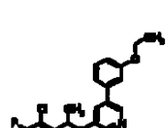
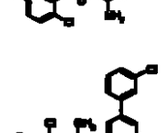
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
I-540		3-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-5-(pyridin-4-ylmethoxy)-pyridin-2-ylamine	0.8	17		392
I-541		(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone	0.079	4 as in Example I-291	(300MHZ, CDCl3) δ 7.89 (s, 1H), 7.40 (m, 4H), 7.35 (dd, 1H), 7.09 (t, 1H), 7.02 (s, 1H), 6.17 (q, 1H), 4.98 (s, 2H), 3.82 (m, 2H), 3.62 (m, 2H), 2.52 (m, 4H), 1.88 (d, 3H).	567

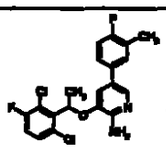
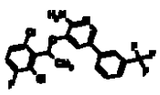
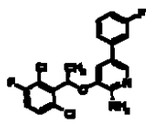
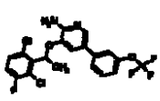
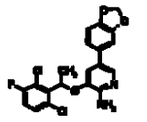
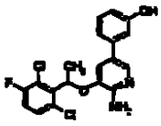
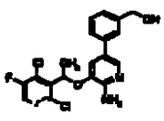
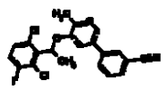
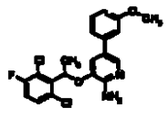
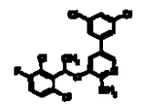
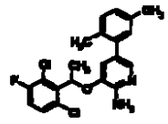
Table 3

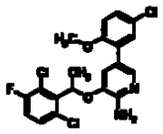
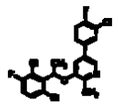
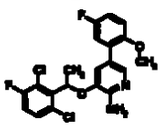
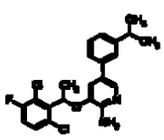
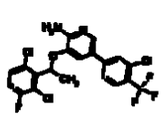
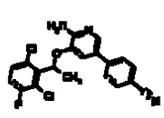
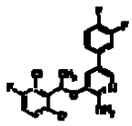
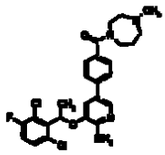
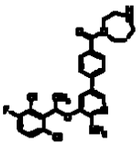
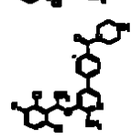
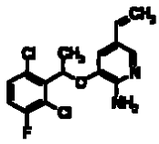
No.	Structure	Name	Ki (μM) or I (%)	^{1}H-NMR	MS m/z (M+H)	Procedure
I-542		(4-{6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone	0.023	(400 MHz, DMSO-D6) d ppm 0.84 (s, 3 H) 0.93 - 1.10 (m, 3 H) 1.60 (d, J=6.57 Hz, 3 H) 2.30 (s, 2 H) 2.65 - 2.74 (m, 2 H) 3.36 - 3.49 (m, 1 H) 4.32 (s, 1 H) 5.96 (s, 2 H) 6.14 (q, J=6.57 Hz, 1 H) 7.00 (d, J=1.77 Hz, 1 H) 7.36 (m, 2 H) 7.46 (m, 3 H) 7.56 (dd, J=6.57, 4.93 Hz, 1 H) 7.68 (d, J=1.77 Hz, 1 H)	517	18/19/20/31
I-543		(4-{6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone	1.6	(400 MHz, DMSO-D6) d ppm 0.84 (s, 3 H) 0.93 - 1.10 (m, 3 H) 1.60 (d, J=6.57 Hz, 3 H) 2.30 (s, 2 H) 2.65 - 2.74 (m, 2 H) 3.36 - 3.49 (m, 1 H) 4.32 (s, 1 H) 5.96 (s, 2 H) 6.14 (q, J=6.57 Hz, 1 H) 7.00 (d, J=1.77 Hz, 1 H) 7.36 (m, 2 H) 7.46 (m, 3 H) 7.56 (dd, J=6.57, 4.93 Hz, 1 H) 7.68 (d, J=1.77 Hz, 1 H)	517	18/19/20/31
I-544		5-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-2-fluoro-benzonitrile		(400 MHz, DMSO-D6) d ppm 1.60 (d, J=6.62 Hz, 3 H) 6.01 (s, 2 H) 6.17 (q, J=6.57 Hz, 1 H) 7.05 (d, J=1.77 Hz, 1 H) 7.44 (t, J=8.72 Hz, 1 H) 7.55 (m, 2 H) 7.79 (m, 1 H) 7.89 (d, J=1.77 Hz, 1 H) 7.97 (dd, J=6.06, 2.27 Hz, 1 H)	420	27
I-545		4-(4-{6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-piperidin-4-ol		(400 MHz, DMSO-D6) d ppm 1.49 - 1.65 (m, 2 H) 1.76 - 1.88 (m, 3 H) 1.88 - 1.98 (m, 3 H) 2.53 (s, 1 H) 2.58 (s, 2 H) 2.69 (s, 2 H) 5.84 (s, 2 H) 6.11 (d, J=6.57 Hz, 1 H) 6.93 (s, 1 H) 7.26 - 7.38 (m, J=8.06 Hz, 2 H) 7.39 - 7.50 (m, J=8.21, 8.21 Hz, 3 H) 7.57 (dd, J=8.72, 4.93 Hz, 1 H) 7.81 (s, 1 H)	477	27
I-546		(4-{6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-piperidin-1-yl-methanone	0.057	(400 MHz, DMSO-D6) d ppm 1.43 - 1.58 (m, 4 H) 1.61(d, J=6.79 Hz, 4 H) 1.81 (d, J=6.57 Hz, 3 H) 3.51 (s, 2 H) 5.84 (s, 2 H) 6.18 (d, J=6.62 Hz, 1 H) 7.00 (d, J=1.77 Hz, 1 H) 7.38 - 7.41 (m, 2 H) 7.40 - 7.50 (m, 3 H) 7.57(dd, J=9.09, 5.05 Hz, 1 H) 7.67 (d, J=2.02 Hz, 1 H)	486	20
I-547		(4-{6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-pyrrolidin-1-yl-methanone	0.067	(400 MHz, DMSO-D6) d ppm 1.73 - 1.93 (m, 7 H) 3.36 - 3.52 (m, 4 H) 5.98 (s, 2 H) 6.07 - 6.20 (m, J=6.62 Hz, 1 H) 6.99 (d, J=1.77 Hz, 1 H) 7.38 - 7.47 (m, 3 H) 7.52 (d, 2 H) 7.58 (dd, J=9.09, 5.05 Hz, 1 H) 7.82 - 7.92 (m, J=1.77 Hz, 1 H)	474	20
I-548		4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-etho.y]-pyridin-3-yl]-3-methyl-benzoic acid methyl ester	17%	(400 MHz, CHLOROFORM-D) d ppm 1.77 - 1.98 (m, 3 H) 2.11 (s, 3 H) 3.91 (s, 3 H) 4.20 (s, 2 H) 6.02 (d, J=6.82 Hz, 1 H) 6.93 (d, J=1.77 Hz, 1 H) 7.00 - 7.09 (m, 1 H) 7.14 (d, J=7.83 Hz, 1 H) 7.28 - 7.31 (m, 1 H) 7.59 (d, J=1.77 Hz, 1 H) 7.83 (dd, J=7.96, 1.39 Hz, 1 H) 7.88 (s, 1 H)	460	19
I-549		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(dimethyl-piperazin-1-ylmethyl)-phenyl]-pyridin-2-ylamine	0.098	(400 MHz, DMSO-D6) d ppm 0.84 - 0.96 (m, 6 H) 1.44 - 1.61 (m, 2 H) 1.72 - 1.83 (m, 3 H) 2.68 - 2.79 (m, 2 H) 2.71 - 2.84 (m, 4 H) 5.79 - 5.92 (m, 2 H) 6.02 - 6.18 (m, 1 H) 6.86 - 7.01 (m, 1 H) 7.25 (d, 2 H) 7.32 (d, 2 H) 7.38 - 7.48 (m, 1 H) 7.50 - 7.64 (m, 2 H) 7.76 - 7.86 (m, 1 H)	503	29
I-550		(4-{6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-3,5-dimethoxy-phenyl)-(dimethyl-piperazin-1-yl)-methanone	18%	(400 MHz, DMSO-D6) d ppm 0.77 - 0.91 (m, 3 H) 1.00 (s, 3 H) 1.75 (d, J=6.62 Hz, 3 H) 2.16 - 2.30 (m, J=12.63 Hz, 3 H) 2.64 - 2.76 (m, 3 H) 3.54 (s, 6 H) 4.25 - 4.40 (m, 1 H) 5.96 (s, 2 H) 5.91 (q, J=6.74 Hz, 1 H) 6.84 - 6.87 (m, 3 H) 7.37 - 7.43 (m, 1 H) 7.43 - 7.51 (m, 1 H) 7.51 - 7.60 (m, 1 H)	577	19/20
I-551		(4-{6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-2-fluoro-phenyl)-(dimethyl-piperazin-1-yl)-methanone	0.091	(400 MHz, DMSO-D6) d ppm 0.80 - 0.96 (m, 3 H) 1.06 (s, 3 H) 1.60 (d, J=6.57 Hz, 3 H) 2.28 - 2.42 (m, J=1.52 Hz, 2 H) 2.61 - 2.85 (m, J=1.77 Hz, 3 H) 4.36 - 4.47 (m, J=8.32 Hz, 1 H) 6.06 (s, 2 H) 6.16 (q, J=6.57 Hz, 1 H) 7.02 (s, 1 H) 7.27 - 7.40 (m, 3 H) 7.40 - 7.49 (m, J=8.72, 8.72 Hz, 2 H) 7.51 - 7.62 (m, J=8.84, 5.05 Hz, 1 H) 7.93 (s, 1 H)	635	19/20

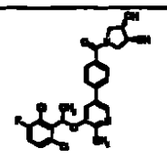
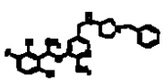
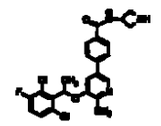
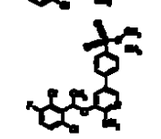
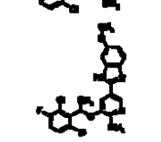
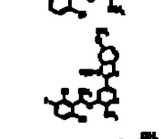
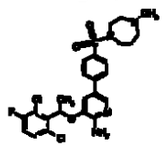
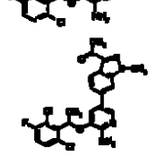
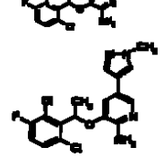
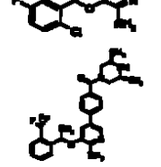
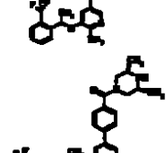
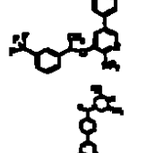
No.	Structure	Name	Ki (μM) or I (%)	^{1}H-NMR	MS m/z (M+H)	Procedure
I-552		(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-3-fluoro-phenyl)-(dimethyl-piperazin-1-yl)-methanone	0.2237	(400 MHz, DMSO-D6) d ppm 0.83 - 1.00 (m, 3 H) 1.02 - 1.17 (m, 3 H) 1.78 (d, 3 H) 2.70 - 2.96 (m, 6 H) 4.38 - 4.50 (m, 1 H) 6.01 - 6.10 (m, 2 H) 6.10 - 6.22 (m, 1 H) 6.96 - 7.04 (m, 1 H) 7.06 - 7.18 (m, 1 H) 7.18 - 7.23 (m, 1 H) 7.30 - 7.39 (m, 1 H) 7.40 - 7.49 (m, 1 H) 7.50 - 7.59 (m, 1 H) 7.86 - 7.96 (m, 1 H)	535	19/20
I-553		(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-3-methyl-phenyl)-(dimethyl-piperazin-1-yl)-methanone	0.2893	(400 MHz, DMSO-D6) d ppm 0.86 (s, 3 H) 1.01 (s, 3 H) 1.77 (d, J=6.57 Hz, 3 H) 1.96 (s, 3 H) 2.31 (s, 1 H) 2.73 (s, 3 H) 3.80 (s, 2 H) 4.35 (s, 1 H) 5.89 (s, 2 H) 6.00 (q, J=6.57 Hz, 1 H) 6.80 (s, 1 H) 7.01 - 7.12 (m, J=7.83 Hz, 1 H) 7.12 - 7.28 (m, 2 H) 7.37 - 7.53 (m, 3 H)	531	19/20
I-554		(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((2R,6S)-2,6-dimethyl-morpholin-4-yl)-methanone	0.1407	(400 MHz, DMSO-D6) d ppm 1.00 - 1.31 (m, 4 H) 1.57 (d, J=6.82 Hz, 3 H) 3.37 - 3.40 (m, 6 H) 3.58 - 3.65 (m, 2 H) 6.01 - 6.08 (m, 2 H) 6.21 (q, J=6.57 Hz, 1 H) 7.07 (d, J=1.77 Hz, 1 H) 7.45 - 7.55 (m, 5 H) 7.83 (dd, J=8.84, 6.06 Hz, 1 H) 7.92 - 7.99 (m, 1 H)	518	19
I-555		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(2-ethoxy-phenyl)-pyridin-2-ylamine	22%	(400 MHz, DMSO-D6) d ppm 1.36 (t, J=6.82 Hz, 3 H) 1.86 (d, J=6.57 Hz, 3 H) 4.08 - 4.16 (m, 2 H) 5.91 - 6.06 (m, 2 H) 6.18 (q, J=6.57 Hz, 1 H) 7.06 - 7.13 (m, 2 H) 7.19 (d, J=7.83 Hz, 1 H) 7.27 (dd, J=7.58, 1.77 Hz, 1 H) 7.40 (t, J=8.59 Hz, 1 H) 7.62 (t, J=8.59 Hz, 1 H) 7.73 (dd, J=8.08, 6.06 Hz, 1 H) 7.84 (d, J=1.77 Hz, 1 H)	421	19
I-556		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(2,5-dimethoxy-phenyl)-pyridin-2-ylamine	0.5749	(400 MHz, DMSO-D6) d ppm 1.22 (d, J=6.57 Hz, 3 H) 3.57 - 3.58 (m, 3 H) 3.74 - 3.78 (m, 3 H) 5.82 - 5.98 (m, 2 H) 6.03 (q, J=6.57 Hz, 1 H) 6.72 (d, J=8.28 Hz, 1 H) 6.84 (dd, J=8.84, 3.03 Hz, 1 H) 6.86 (d, J=1.77 Hz, 1 H) 6.96 (d, J=9.09 Hz, 1 H) 7.50 (t, J=8.59 Hz, 1 H) 7.81 (dd, J=8.84, 4.80 Hz, 1 H) 7.88 (d, J=1.77 Hz, 1 H)	437	19
I-557		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(2,4-dimethoxy-phenyl)-pyridin-2-ylamine	0.2172	(400 MHz, DMSO-D6) d ppm 1.83 (d, J=6.82 Hz, 3 H) 3.64 - 3.67 (m, 3 H) 3.81 - 3.84 (m, 3 H) 5.74 - 5.78 (m, 2 H) 6.03 (q, J=6.57 Hz, 1 H) 6.59 (dd, J=8.34, 2.27 Hz, 1 H) 6.64 (d, J=2.53 Hz, 1 H) 6.88 (d, J=1.77 Hz, 1 H) 7.10 (d, J=8.34 Hz, 1 H) 7.53 (t, J=8.59 Hz, 1 H) 7.56 (d, J=1.77 Hz, 1 H) 7.89 (dd, J=8.84, 6.06 Hz, 1 H)	437	19
I-558		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(2,5-dimethoxy-phenyl)-pyridin-2-ylamine	2%	(400 MHz, DMSO-D6) d ppm 1.81 (d, J=6.82 Hz, 3 H) 3.58 - 3.59 (m, 6 H) 5.86 - 5.89 (m, 2 H) 5.98 (q, J=6.82 Hz, 1 H) 6.63 (d, J=1.77 Hz, 1 H) 6.71 (d, J=8.34 Hz, 2 H) 7.28 (t, J=8.34 Hz, 1 H) 7.42 (d, J=1.52 Hz, 1 H) 7.82 (t, J=8.59 Hz, 1 H) 7.91 (dd, J=8.84, 6.06 Hz, 1 H)	437	19
I-559		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(2-trifluoromethyl-phenyl)-pyridin-2-ylamine	4%	(400 MHz, DMSO-D6) d ppm 1.78 (d, J=6.57 Hz, 3 H) 5.91 - 6.09 (m, 3 H) 6.59 - 6.60 (m, 1 H) 7.28 (d, J=7.58 Hz, 1 H) 7.42 - 7.48 (m, 2 H) 7.50 - 7.58 (m, 2 H) 7.65 (t, J=7.33 Hz, 1 H) 7.75 (d, J=7.83 Hz, 1 H)	445	19
I-560		5-(2-Chloro-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine	24%	(400 MHz, DMSO-D6) d ppm 1.79 (d, J=6.82 Hz, 3 H) 5.96 - 6.03 (m, 3 H) 6.75 (d, J=1.77 Hz, 1 H) 7.27 - 7.38 (m, 3 H) 7.42 - 7.49 (m, 2 H) 7.52 - 7.57 (m, 2 H)	411	19
I-561		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(2-trifluoromethoxy-phenyl)-pyridin-2-ylamine	14%	(400 MHz, DMSO-D6) d ppm 1.74 (d, J=6.82 Hz, 3 H) 5.92 - 5.98 (m, 3 H) 6.74 (d, J=1.77 Hz, 1 H) 7.29 - 7.43 (m, 5 H) 7.50 (dd, J=9.09, 6.06 Hz, 1 H) 7.86 (d, J=1.77 Hz, 1 H)	461	19
I-562		1-(2-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-ethanone	6%	(400 MHz, DMSO-D6) d ppm 1.83 (d, J=6.82 Hz, 3 H) 1.92 - 1.93 (m, 3 H) 6.01 - 6.07 (m, 3 H) 6.69 (d, J=2.02 Hz, 1 H) 7.26 (d, J=7.83 Hz, 1 H) 7.46 (t, J=7.33 Hz, 1 H) 7.49 - 7.51 (m, 1 H) 7.52 - 7.58 (m, 3 H) 7.91 (dd, J=8.84, 6.06 Hz, 1 H)	418	19

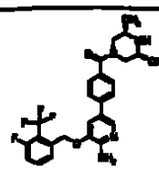
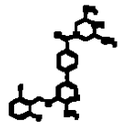
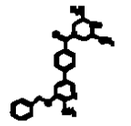
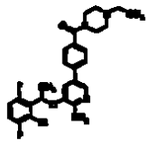
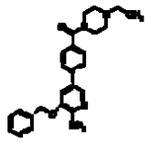
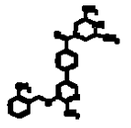
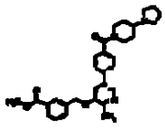
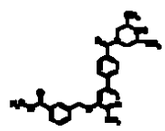
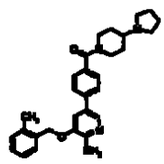
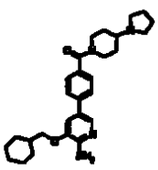
No.	Structure	Name	Ki (μM) or I (%)	^{1}H-NMR	MS m/z (M+H)	Procedure
I-563		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-6-(2-fluoro-phenyl)-pyridin-2-ylamine	0.4322	(400 MHz, DMSO-D6) d ppm 1.71 (d, J=6.57 Hz, 3 H) 5.88 - 5.90 (m, 2 H) 6.96 (q, J=6.82 Hz, 1 H) 6.76 - 6.78 (m, 1 H) 7.10 - 7.16 (m, 2 H) 7.19 - 7.38 (m, 2 H) 7.38 (t, J=8.08 Hz, 1 H) 7.47 (dd, J=8.84, 4.80 Hz, 1 H) 7.60 - 7.63 (m, 1 H)	395	19
I-564		(2-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-methanol	21%	(400 MHz, DMSO-D6) d ppm 1.79 (d, J=6.57 Hz, 3 H) 4.20 (t, J=5.05 Hz, 2 H) 5.03 (t, J=5.56 Hz, 1 H) 5.82 - 5.83 (m, 2 H) 6.02 (q, J=6.57 Hz, 1 H) 6.66 (d, J=1.77 Hz, 1 H) 7.01 (dd, J=7.58, 1.52 Hz, 1 H) 7.25 (dt, J=7.58, 1.52 Hz, 1 H) 7.31 (dt, J=7.33, 1.26 Hz, 1 H) 7.46 (t, J=8.59 Hz, 1 H) 7.49 - 7.53 (m, 2 H) 7.58 (dd, J=8.84, 5.06 Hz, 1 H)	407	19
I-565		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-6-o-tolyl-pyridin-2-ylamine	25%	(400 MHz, DMSO-D6) d ppm 1.66 (d, J=6.57 Hz, 3 H) 1.80 - 1.80 (m, 3 H) 5.87 - 5.89 (m, 2 H) 6.66 (q, J=6.57 Hz, 1 H) 6.45 (d, J=1.77 Hz, 1 H) 6.86 - 6.90 (m, 1 H) 7.00 - 7.09 (m, 3 H) 7.29 - 7.36 (m, 2 H) 7.42 (dd, J=8.84, 6.06 Hz, 1 H)	391	19
I-566		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-6-(2-methoxy-phenyl)-pyridin-2-ylamine	0.2779	(400 MHz, DMSO-D6) d ppm 1.84 (d, J=6.57 Hz, 3 H) 3.85 - 3.86 (m, 3 H) 5.83 - 5.84 (m, 2 H) 6.04 (q, J=6.57 Hz, 1 H) 6.63 (d, J=1.77 Hz, 1 H) 7.00 (dt, J=7.33, 1.01 Hz, 1 H) 7.08 (d, J=7.83 Hz, 1 H) 7.19 (dd, J=7.58, 1.77 Hz, 1 H) 7.29 - 7.34 (m, 1 H) 7.53 (t, J=8.84 Hz, 1 H) 7.61 - 7.66 (m, 2 H)	407	19
I-567		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-6-(2,6-dimethyl-phenyl)-pyridin-3-ylamine	0%	(400 MHz, DMSO-D6) d ppm 1.67 - 1.68 (m, 3 H) 1.79 (d, J=6.82 Hz, 3 H) 1.87 - 1.88 (m, 3 H) 5.73 - 5.75 (m, 2 H) 5.98 (q, J=6.57 Hz, 1 H) 6.41 (d, J=1.77 Hz, 1 H) 6.99 - 7.11 (m, 3 H) 7.25 (d, J=1.77 Hz, 1 H) 7.44 (t, J=8.59 Hz, 1 H) 7.84 (dd, J=8.84, 6.06 Hz, 1 H)	405	19
I-568		(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-morpholin-4-yl-methanone	0.0825	Anal. Calcd for C24 H22 Cl2 F N3 O3: C, 58.79; H, 4.52; N, 8.57. Found: C, 58.39; H, 4.72; N, 8.24.	490	20
I-569		(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-3-chloro-phenyl)-((3R,5S)-dimethyl-piperazin-1-yl)-methanone	0.0478	Anal. Calcd for C28 H28 Cl3 F N4 O2: C, 56.69; H, 4.75; N, 10.15. Found: C, 52.83; H, 5.16; N, 8.72. 1.1eq of H20; 1.3 eq AcOH	551	19/20
I-570		4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-2-methyl-phenyl)-((3R,5S)-dimethyl-piperazin-1-yl)-methanone	0.1225	Anal. Calcd for C27 H29 Cl2 F N4 O2: C, 61.02; H, 5.50; N, 10.54. Found: C, 55.99; H, 5.79; N, 9.01. 1.2eq of H20; 1.6eq of AcOH	531	19/20
I-571		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-6-[4-((2R,6S)-2,6-dimethyl-morpholin-4-ylmethyl)-phenyl]-pyridin-2-ylamine	0.2204	(400 MHz, CHLOROFORM-D) d ppm 1.09 (d, J=6.32 Hz, 6 H) 1.80 (d, J=6.82 Hz, 3 H) 1.88 - 1.98 (m, 2 H) 2.78 - 2.90 (m, 2 H) 3.59 - 3.70 (m, 2 H) 3.86 - 3.95 (m, 2 H) 5.12 - 5.16 (m, 2 H) 6.06 (q, J=6.57 Hz, 1 H) 6.94 - 7.04 (m, 2 H) 7.25 (dd, J=8.84, 4.80 Hz, 1 H) 7.26 - 7.34 (m, 2 H) 7.39 - 7.44 (m, 2 H) 7.77 (d, J=1.52 Hz, 1 H)	504	28
I-572		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-6-(4-morpholin-4-ylmethyl-phenyl)-pyridin-2-ylamine	0.0554	(400 MHz, CHLOROFORM-D) d ppm 1.80 (d, J=6.57 Hz, 3 H) 2.51 - 2.58 (m, 4 H) 3.58 - 3.60 (m, 2 H) 3.75 (t, J=4.55 Hz, 4 H) 5.27 - 5.31 (m, 2 H) 6.06 (q, J=6.57 Hz, 1 H) 6.66 (d, J=1.52 Hz, 1 H) 7.00 (t, J=8.08 Hz, 1 H) 7.22 - 7.29 (m, 3 H) 7.53 - 7.57 (m, 2 H) 7.74 (d, J=1.77 Hz, 1 H)	476	28
I-573		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-6-(2,6-dimethyl-phenyl)-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.64 (d, J=6.57 Hz, 3 H) 2.08 - 2.10 (m, 6 H) 5.85 - 5.88 (m, 2 H) 5.93 (q, J=6.57 Hz, 1 H) 6.69 - 6.71 (m, 2 H) 6.76 - 6.78 (m, 2 H) 7.28 (t, J=8.59 Hz, 1 H) 7.40 (dd, J=8.09, 4.80 Hz, 1 H) 7.82 (d, J=1.77 Hz, 1 H)	405	19

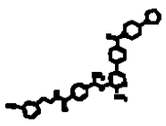
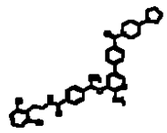
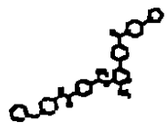
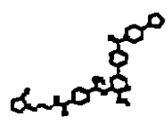
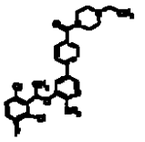
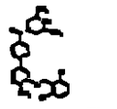
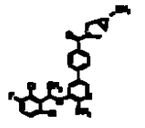
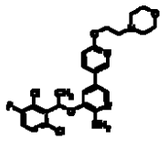
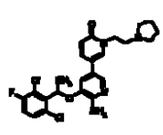
No.	Structure	Name	Ki (uM) or I (%)	^{1}H-NMR	MS m/z (M+H)	Procedure
I-574		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-m-tolyl-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.78 (d, J=6.57 Hz, 3 H) 2.27 - 2.28 (m, 3 H) 5.80 - 5.84 (m, 2 H) 6.08 (q, J=6.57 Hz, 1 H) 6.88 (d, J=1.77 Hz, 1 H) 7.02 (d, J=7.33 Hz, 1 H) 7.09 - 7.15 (m, 2 H) 7.21 (t, J=7.58 Hz, 1 H) 7.41 (t, J=8.59 Hz, 1 H) 7.64 (dd, J=8.08, 6.06 Hz, 1 H) 7.77 (d, J=1.77 Hz, 1 H)	391	19
I-575		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-6-(3,4-dimethoxy-phenyl)-pyridin-3-ylamine		(400 MHz, DMSO-D6) d ppm 1.80 (d, J=6.57 Hz, 3 H) 3.85 (d, J=14.91 Hz, 6 H) 5.57 - 5.60 (m, 2 H) 6.00 (q, J=6.57 Hz, 1 H) 6.83 (d, J=2.02 Hz, 1 H) 6.85 (d, J=1.77 Hz, 1 H) 6.86 - 6.78 (m, 2 H) 7.23 (t, J=8.59 Hz, 1 H) 7.38 (dd, J=4.80, 4.04 Hz, 1 H) 7.86 (d, J=1.77 Hz, 1 H)	437	19
I-576		5-Biphenyl-3-yl-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.83 (d, J=6.57 Hz, 3 H) 5.92 - 5.95 (m, 2 H) 6.16 (q, J=6.57 Hz, 1 H) 7.01 (d, J=1.52 Hz, 1 H) 7.35 - 7.59 (m, 9 H) 7.68 (d, J=7.33 Hz, 2 H) 7.93 (d, J=1.52 Hz, 1 H)	453	19
I-577		5-(3,5-Bis-trifluoromethyl-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.84 (d, J=6.57 Hz, 3 H) 6.16 - 6.24 (m, 3 H) 7.03 (d, J=1.77 Hz, 1 H) 7.45 (t, J=8.59 Hz, 1 H) 7.64 (dd, J=8.08, 6.06 Hz, 1 H) 7.92 - 7.96 (m, 1 H) 8.00 - 8.02 (m, 2 H) 8.06 (d, J=2.02 Hz, 1 H)	513	19
I-578		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-6-(3,4-dichloro-phenyl)-pyridin-3-ylamine		(400 MHz, DMSO-D6) d ppm 1.87 (d, J=6.57 Hz, 3 H) 6.09 - 6.12 (m, 2 H) 6.22 (q, J=6.57 Hz, 1 H) 7.04 (d, J=1.77 Hz, 1 H) 7.46 - 7.53 (m, 2 H) 7.62 (dd, J=8.08, 6.06 Hz, 1 H) 7.69 - 7.70 (m, 2 H) 7.99 (d, J=2.02 Hz, 1 H)	446	19
I-579		1-(3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-ethanone		(400 MHz, DMSO-D6) d ppm 1.76 (d, J=6.57 Hz, 3 H) 2.54 - 2.56 (m, 3 H) 5.90 - 5.94 (m, 2 H) 6.10 (q, J=6.57 Hz, 1 H) 6.93 (d, J=1.77 Hz, 1 H) 7.39 (t, J=8.59 Hz, 1 H) 7.46 (t, J=7.83 Hz, 1 H) 7.61 (dd, J=8.08, 6.06 Hz, 1 H) 7.83 (d, J=8.34 Hz, 1 H) 7.76 (d, J=7.83 Hz, 1 H) 7.81 - 7.83 (m, 1 H) 7.88 (d, J=2.02 Hz, 1 H)	419	19
I-580		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-6-(3,5-difluoro-phenyl)-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.82 (d, J=6.57 Hz, 3 H) 6.08 - 6.10 (m, 2 H) 6.15 (q, J=6.57 Hz, 1 H) 7.01 (d, J=1.77 Hz, 1 H) 7.08 - 7.19 (m, 3 H) 7.46 (t, J=8.84 Hz, 1 H) 7.58 (dd, J=8.09, 6.05 Hz, 1 H) 7.95 (d, J=2.02 Hz, 1 H)	413	19
I-581		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-6-(2,6-dichloro-phenyl)-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.90 (d, J=6.82 Hz, 3 H) 6.10 (q, J=6.57 Hz, 1 H) 6.17 - 6.19 (m, 2 H) 6.84 (d, J=1.77 Hz, 1 H) 7.44 - 7.51 (m, 2 H) 7.66 (t, J=8.59 Hz, 1 H) 7.69 - 7.70 (m, 3 H)	446	19
I-582		(4-[5-Amino-6-[1-(2,6-dichloro-4-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone		Passed CHN 1.0eq AcOH	567	18/20
I-583		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-6-(3-ethoxy-phenyl)-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.35 (t, J=6.82 Hz, 3 H) 1.82 (d, J=6.57 Hz, 3 H) 3.99 - 4.09 (m, 2 H) 5.88 - 5.91 (m, 2 H) 6.13 (q, J=6.57 Hz, 1 H) 6.80 (dd, J=8.08, 2.27 Hz, 1 H) 6.84 (t, J=2.02 Hz, 1 H) 6.92 (d, J=1.77 Hz, 1 H) 6.96 (d, J=7.58 Hz, 1 H) 7.26 (t, J=7.83 Hz, 1 H) 7.46 (t, J=8.59 Hz, 1 H) 7.57 (dd, J=8.84, 8.08 Hz, 1 H) 7.83 (d, J=1.77 Hz, 1 H)	421	19
I-584		5-(3-Chloro-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.87 (d, J=6.57 Hz, 3 H) 6.03 - 6.06 (m, 2 H) 6.18 - 6.24 (m, 1 H) 7.02 (d, J=2.02 Hz, 1 H) 7.35 (td, J=8.82, 1.77 Hz, 1 H) 7.41 - 7.53 (m, 4 H) 7.82 (dd, J=8.84, 6.06 Hz, 1 H) 7.93 (d, J=2.02 Hz, 1 H)	411	19

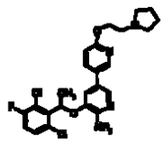
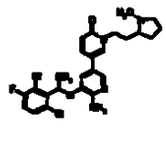
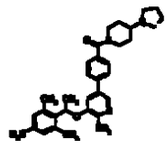
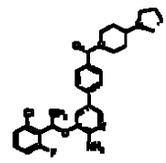
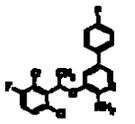
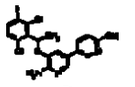
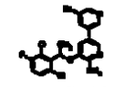
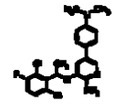
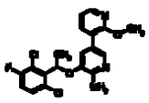
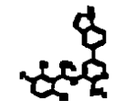
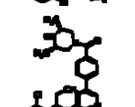
No.	Structure	Name	KI (μM) or I (%)	^{1}H-NMR	MS m/z (M+H)	Procedure
I-555		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(4-fluoro-3-methyl-phenyl)-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.58 (d, J=6.57 Hz, 3 H) 2.01 - 2.02 (m, 3 H) 5.62 - 5.64 (m, 2 H) 6.09 (q, J=6.82 Hz, 1 H) 6.66 (d, J=1.77 Hz, 1 H) 6.90 (t, J=8.84 Hz, 1 H) 6.99 - 7.04 (m, 2 H) 7.22 (t, J=8.59 Hz, 1 H) 7.34 (dd, J=8.09, 5.05 Hz, 1 H) 7.56 (d, J=1.77 Hz, 1 H)	409	19
I-556		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-trifluoromethyl-phenyl)-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.64 (d, J=6.57 Hz, 3 H) 6.05 - 6.07 (m, 2 H) 6.14 - 6.21 (m, 1 H) 6.66 (d, J=1.77 Hz, 1 H) 7.46 (t, J=8.59 Hz, 1 H) 7.56 (dd, J=8.84, 5.05 Hz, 1 H) 7.69 - 7.88 (m, 3 H) 7.76 - 7.80 (m, 1 H) 7.95 (d, J=1.77 Hz, 1 H)	445	19
I-557		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-fluoro-phenyl)-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.62 (d, J=6.57 Hz, 3 H) 5.98 - 6.00 (m, 2 H) 6.13 - 6.20 (m, 1 H) 6.69 (d, J=1.77 Hz, 1 H) 7.05 - 7.11 (m, 1 H) 7.21 - 7.27 (m, 2 H) 7.39 - 7.49 (m, 2 H) 7.59 (dd, J=8.09, 5.05 Hz, 1 H) 7.90 (d, J=2.02 Hz, 1 H)	395	19
I-558		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-trifluoromethoxy-phenyl)-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.60 (d, J=6.57 Hz, 3 H) 5.80 - 5.84 (m, 2 H) 5.90 - 5.96 (m, 1 H) 6.73 (d, J=2.02 Hz, 1 H) 7.00 - 7.07 (m, 2 H) 7.20 - 7.30 (m, 3 H) 7.34 (dd, J=8.84, 4.80 Hz, 1 H) 7.88 (d, J=1.77 Hz, 1 H)	461	19
I-559		5-Benzo[1,3]dioxol-5-yl-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.62 (d, J=6.57 Hz, 3 H) 5.81 - 5.83 (m, 2 H) 6.03 - 6.04 (m, 2 H) 6.10 - 6.17 (m, 1 H) 6.83 - 6.96 (m, 4 H) 7.46 (t, J=8.84 Hz, 1 H) 7.59 (dd, J=8.09, 5.05 Hz, 1 H) 7.79 (d, J=2.02 Hz, 1 H)	421	19
I-560		3-[5-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenol		(400 MHz, DMSO-D6) d ppm 1.95 (d, J=6.82 Hz, 3 H) 5.98 - 6.00 (m, 2 H) 6.22 - 6.28 (m, 1 H) 6.78 - 6.81 (m, 1 H) 6.89 - 6.93 (m, 2 H) 7.04 (d, J=1.77 Hz, 1 H) 7.29 (t, J=8.08 Hz, 1 H) 7.58 (t, J=8.08, 8.59 Hz, 1 H) 7.71 (dd, J=8.84, 4.80 Hz, 1 H) 7.89 (d, J=1.77 Hz, 1 H) 9.56 - 9.57 (m, 1 H)	393	19
I-561		[3-[5-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl]-methanol		(400 MHz, DMSO-D6) d ppm 1.63 (d, J=6.57 Hz, 3 H) 4.52 (d, J=5.31 Hz, 2 H) 5.18 - 5.22 (m, 1 H) 5.58 - 5.60 (m, 2 H) 6.11 - 6.17 (m, 1 H) 6.68 (d, J=1.52 Hz, 1 H) 7.20 - 7.29 (m, 2 H) 7.31 - 7.36 (m, 2 H) 7.46 (t, J=8.84 Hz, 1 H) 7.58 (dd, J=8.09, 5.05 Hz, 1 H) 7.83 (d, J=1.77 Hz, 1 H)	407	19
I-562		3-[5-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzonitrile		(400 MHz, DMSO-D6) d ppm 1.63 (d, J=6.57 Hz, 3 H) 6.10 - 6.12 (m, 2 H) 6.24 (q, J=6.57 Hz, 1 H) 7.12 (d, J=1.77 Hz, 1 H) 7.61 (t, J=8.59 Hz, 1 H) 7.80 - 7.86 (m, 2 H) 7.77 (d, J=7.83 Hz, 1 H) 7.81 (d, J=8.08 Hz, 1 H) 7.84 - 7.86 (m, 1 H) 8.00 (d, J=1.77 Hz, 1 H)	402	19
I-563		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-methoxy-phenyl)-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.63 (d, J=6.57 Hz, 3 H) 3.79 - 3.80 (m, 3 H) 5.91 - 5.92 (m, 2 H) 6.11 - 6.18 (m, 1 H) 6.81 - 6.84 (m, 1 H) 6.86 - 6.89 (m, 1 H) 6.93 (d, J=1.52 Hz, 1 H) 6.97 - 7.01 (m, 1 H) 7.29 (t, J=8.34, 7.83 Hz, 1 H) 7.46 (t, J=8.84 Hz, 1 H) 7.59 (dd, J=8.08, 5.05 Hz, 1 H) 7.88 (d, J=1.77 Hz, 1 H)	407	19
I-564		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(3,5-dichloro-phenyl)-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.63 (d, J=6.57 Hz, 3 H) 6.10 - 6.12 (m, 2 H) 6.18 - 6.22 (m, 1 H) 7.00 (d, J=1.77 Hz, 1 H) 7.44 - 7.49 (m, 4 H) 7.58 (dd, J=8.08, 5.31 Hz, 1 H) 7.86 (d, J=2.02 Hz, 1 H)	446	19
I-565		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(2,5-dimethyl-phenyl)-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.60 (d, J=6.82 Hz, 3 H) 1.90 - 1.93 (m, 3 H) 2.24 - 2.27 (m, 3 H) 5.81 - 5.83 (m, 2 H) 6.00 (q, J=6.82, 6.32 Hz, 1 H) 6.57 (d, J=1.77 Hz, 1 H) 6.79 - 6.82 (m, 1 H) 6.96 - 7.03 (m, 1 H) 7.10 (d, J=7.83 Hz, 1 H) 7.45 - 7.52 (m, 2 H) 7.58 (dd, J=8.84, 5.05 Hz, 1 H)	405	19

No.	Structure	Name	KI (μM) or I (%)	^{1}H-NMR	MS m/z (M+H)	Procedure
I-596		5-(5-Chloro-2-methoxy-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.79 (d, J=6.57 Hz, 3 H) 3.61 - 3.63 (m, 3 H) 5.89 - 5.91 (m, 2 H) 6.97 - 8.03 (m, 1 H) 6.86 (d, J=1.77 Hz, 1 H) 7.06 (d, J=8.84 Hz, 1 H) 7.15 (d, J=2.78 Hz, 1 H) 7.29 (dd, J=8.84, 2.53 Hz, 1 H) 7.49 (t, J=8.59 Hz, 1 H) 7.59 (dd, J=8.08, 5.31 Hz, 1 H) 7.63 (d, J=1.77 Hz, 1 H)	441	19
I-597		5-(3-Chloro-4-fluoro-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.83 (d, J=6.57 Hz, 3 H) 5.98 - 6.00 (m, 2 H) 6.14 - 6.20 (m, 1 H) 6.98 (d, J=1.77 Hz, 1 H) 7.42 - 7.45 (m, 2 H) 7.47 (d, J=8.59 Hz, 1 H) 7.85 - 7.80 (m, 2 H) 7.87 (d, J=2.02 Hz, 1 H)	429	19
I-598		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(5-fluoro-2-methoxy-phenyl)-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.79 (d, J=6.57 Hz, 3 H) 3.69 - 3.80 (m, 3 H) 5.88 - 5.91 (m, 2 H) 6.00 (q, J=6.82 Hz, 1 H) 6.90 (d, J=1.77 Hz, 1 H) 6.99 - 7.10 (m, 3 H) 7.48 (t, J=8.84 Hz, 1 H) 7.59 (dd, J=8.08, 5.31 Hz, 1 H) 7.64 (d, J=2.02 Hz, 1 H)	425	19
I-599		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-isopropyl-phenyl)-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.20 - 1.25 (m, 6 H) 1.83 (d, J=6.57 Hz, 3 H) 2.88 - 2.94 (m, 1 H) 5.88 - 5.91 (m, 2 H) 6.13 (q, J=6.32 Hz, 1 H) 6.89 (d, J=1.77 Hz, 1 H) 7.11 - 7.16 (m, 2 H) 7.23 - 7.31 (m, 2 H) 7.47 (t, J=8.59 Hz, 1 H) 7.58 (dd, J=8.84, 4.80 Hz, 1 H) 7.83 (d, J=2.02 Hz, 1 H)	419	19
I-600		5-(3-Chloro-4-trifluoromethyl-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.83 (d, J=6.57 Hz, 3 H) 6.11 - 6.13 (m, 2 H) 6.17 (q, J=6.57 Hz, 1 H) 6.99 (d, J=1.77 Hz, 1 H) 7.48 (t, J=8.84 Hz, 1 H) 7.58 (dd, J=8.09, 5.05 Hz, 1 H) 7.68 (d, J=1.77 Hz, 1 H) 7.72 (d, J=8.59 Hz, 1 H) 7.80 (dd, J=8.34, 1.77 Hz, 1 H) 7.95 (d, J=2.02 Hz, 1 H)	479.90	19
I-601		4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzonitrile		(400 MHz, DMSO-D6) d ppm 1.83 (d, J=6.57 Hz, 3 H) 6.13 - 6.22 (m, 3 H) 7.09 (d, J=1.77 Hz, 1 H) 7.45 (t, J=8.59 Hz, 1 H) 7.57 (dd, J=8.09, 5.05 Hz, 1 H) 7.83 (d, J=8.59 Hz, 2 H) 7.84 (d, J=8.59 Hz, 2 H) 7.97 (d, J=1.77 Hz, 1 H)	402	19
I-602		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(3,4-difluoro-phenyl)-pyridin-2-ylamine		(400 MHz, DMSO-D6) d ppm 1.82 (d, J=6.82 Hz, 3 H) 5.98 - 6.00 (m, 2 H) 6.17 (q, J=6.57 Hz, 1 H) 6.99 (d, J=1.77 Hz, 1 H) 7.22 - 7.27 (m, 1 H) 7.41 - 7.52 (m, 3 H) 7.58 (dd, J=9.09, 5.05 Hz, 1 H) 7.97 (d, J=2.02 Hz, 1 H)	413	19
I-603		(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-methyl-[1,4]diazepan-1-yl)-methanone	0.0098	(400 MHz, DMSO-D6) d ppm 1.73 (m, 1 H) 1.80 (d, J=6.82 Hz, 3 H) 1.84 (m, 1 H) 2.25 (d, J=21.96 Hz, 2 H) 2.53 (m, 2 H) 2.63 (m, 2H) 3.40 (m, 2 H) 3.60 (m, 2 H) 5.95 (s, 2 H) 6.14 (d, J=6.57 Hz, 1 H) 6.99 (s, 1 H) 7.36 (d, J=7.58 Hz, 2 H) 7.44 (m, 3 H) 7.57 (dd, J=8.97, 4.93 Hz, 1 H) 7.86 (d, J=1.77 Hz, 1 H)	517	20
I-604		(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-[1,4]diazepan-1-yl-methanone	0.031	(400 MHz, DMSO-D6) d ppm 1.81 (t, J=6.19 Hz, 3 H) 1.90 (m, 2 H) 2.96 (m, 2 H) 3.10 (d, J=36.86 Hz, 2 H) 3.45 (m, 2 H) 3.7 (m, 2 H) 5.96 (s, 2 H) 6.14 (q, J=6.82 Hz, 1 H) 6.99 (d, J=1.52 Hz, 1 H) 7.44 (m, 5 H) 7.56 (dd, J=8.97, 4.93 Hz, 1 H) 7.87 (d, J=1.77 Hz, 1 H)	503	20/21
I-605		(4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-piperazin-1-yl-methanone	0.0475	(400 MHz, DMSO-D6) d ppm 1.80 (d, J=6.57 Hz, 3 H) 2.72 (m, 4 H) 3.36 (m, 2 H) 3.62 (m, 2 H) 5.96 (s, 2 H) 6.14 (q, J=6.74 Hz, 1 H) 6.99 (d, J=1.77 Hz, 1 H) 7.37 (m, 2 H) 7.44 (m, 3 H) 7.57 (dd, J=8.97, 4.93 Hz, 1 H) 7.87 (d, J=1.77 Hz, 1 H)	489	20/21
I-606		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-vinyl-pyridin-2-ylamine	0.655	(400 MHz, CHLOROFORM-D) d ppm 1.83 (d, J=6.57 Hz, 3 H) 4.94 (s, 2 H) 5.03 (d, J=11.12 Hz, 1 H) 5.38 (d, J=17.43 Hz, 1 H) 6.06 (q, J=6.82 Hz, 1 H) 6.49 (dd, J=17.68, 10.86 Hz, 1 H) 6.90 (d, J=1.77 Hz, 1 H) 7.04 (dd, J=8.84, 7.83 Hz, 1 H) 7.29 (dd, J=8.84, 4.80 Hz, 1 H) 7.86 (d, J=1.77 Hz, 1 H)	327	19

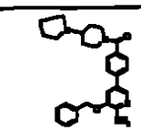
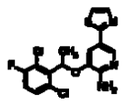
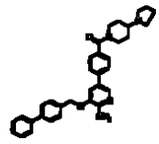
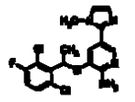
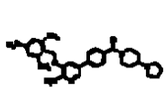
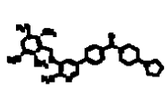
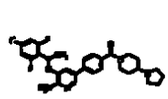
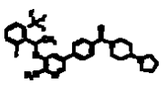
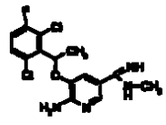
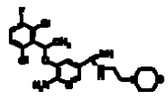
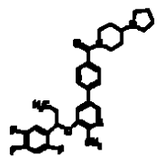
No.	Structure	Name	Ki (μM) or I (%)	^{1}H-NMR	MS m/z (M+H)	Procedure
I-607		(4-{6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,4S)-3,4-dihydroxy-pyrrolidin-1-yl)-methanone	0.066	(400 MHz, DMSO-D6) d ppm 1.81 (d, J=6.82 Hz, 3 H) 3.38 (m, 2 H) 3.54 (m, 2 H) 3.97 (d, J=4.04 Hz, 2 H) 4.06 (d, J=4.29 Hz, 2 H) 5.10 (br, 2 H) 6.98 (d, 2 H) 7.00 (d, J=1.77 Hz, 1 H) 7.45 (m, 3 H) 7.48 (m, 2 H) 7.57 (dd, J=8.97, 4.93 Hz, 1 H) 7.66 (d, J=1.77 Hz, 1 H)	508	20/21
I-608		5-[(1-Benzyl-pyrrolidin-3-ylamino)-methyl]-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine	0%	(400 MHz, DMSO-D6) d ppm 1.34 (m, 1 H) 1.74 (d, J=6.84 Hz, 3 H) 1.76 (m, 1 H) 2.08 (m, 1 H) 2.40 (m, 2 H) 2.54 (m, 1 H) 2.69 (m, 1 H) 3.33 (s, 2 H) 3.49 (s, 2 H) 5.62 (s, 2 H) 5.94 (q, J=6.57 Hz, 1 H) 6.69 (s, 1 H) 7.27 (m, 5 H) 7.39 (m, 1 H) 7.39 (m, 1 H) 7.48 (m, 1 H)	489	23
I-609		4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N-azetidin-3-yl-benzamide	0.048	(400 MHz, DMSO-D6) d ppm 1.80 (d, J=6.57 Hz, 3 H) 2.57 (m, 1 H) 3.43 (m, 1 H) 3.81 (m, 2 H) 4.74 (m, 1 H) 6.00 (s, 2H) 6.13 (q, J=6.48 Hz, 1 H) 6.96 (dd, J=6.57, 1.77 Hz, 1 H) 7.45 (m, 3 H) 7.54 (dd, J=6.97, 4.93 Hz, 1 H) 7.87 (m, 3 H)	475	20/21
I-610		4-[6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-N,N-dimethyl-benzenesulfonamide	0.089	(400 MHz, CHLOROFORM-D) d ppm 1.87 (d, J=6.82 Hz, 3 H) 2.72 (s, 6 H) 4.69 (s, 2 H) 6.12 (q, J=6.57 Hz, 1 H) 6.89 (d, J=1.77 Hz, 1 H) 7.07 (m, 1 H) 7.32 (dd, J=8.84, 4.80 Hz, 1 H) 7.50 (m, 2 H) 7.76 (d, J=8.59 Hz, 2 H) 7.91 (d, J=1.77 Hz, 1 H)	484	29
I-611		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(6-methoxy-1H-benzoimidazol-2-yl)-pyridin-2-ylamine		(400 MHz, MeOD) d ppm 1.72 (d, J=6.57 Hz, 3 H) 3.89 (s, 3 H) 4.76 (s, 2 H) 6.13 (q, J=6.57 Hz, 1 H) 6.71 (dd, J=8.84, 2.27 Hz, 1 H) 6.89 (d, J=2.02 Hz, 1 H) 7.04 (m, 1 H) 7.29 (m, 2 H) 7.40 (d, J=1.77 Hz, 1 H) 8.05 (d, J=2.02 Hz, 1 H)	447	24
I-612		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(6-methoxy-1-methyl-1H-benzoimidazol-2-yl)-pyridin-2-ylamine		(400 MHz, MeOD) d ppm 1.78 (d, J=6.57 Hz, 3 H) 3.51 (s, 3 H) 3.78 (s, 3 H) 6.10 (q, J=6.32 Hz, 1 H) 6.80 (m, 1 H) 6.82 (m, 1 H) 7.13 (m, 1 H) 7.35 (m, 2 H) 7.80 (d, J=7.83 Hz, 1 H)	461	24
I-613		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(4-methyl-[1,4]diazepane-1-sulfonyl)-phenyl]-pyridin-2-ylamine		(400 MHz, MeOD) d ppm 1.83 (m, 2 H) 1.87 (d, J=6.57 Hz, 3 H) 2.66 (m, 4 H) 3.35 (m, 2 H) 3.40 (m, 2 H) 6.20 (q, J=6.65 Hz, 1 H) 7.02 (d, J=1.77 Hz, 1 H) 7.20 (t, J=8.59 Hz, 1 H) 7.43 (dd, J=8.97, 4.93 Hz, 1 H) 7.64 (d, J=8.34 Hz, 2 H) 7.77 (d, J=8.59 Hz, 2 H) 7.81 (d, J=1.26 Hz, 1 H)	583	28
I-614		6-(6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-1-methyl-1H-indazole-3-carboxylic acid amide		(400 MHz, DMSO-D6) d ppm 1.82 (d, J=6.57 Hz, 3 H) 3.92 (s, 3 H) 5.98 (s, 2 H) 6.17 (q, J=6.48 Hz, 1 H) 7.03 (d, J=1.77 Hz, 1 H) 7.36 (dd, J=8.59, 1.26 Hz, 1 H) 7.44 (t, J=8.72 Hz, 1 H) 7.58 (m, 2 H) 7.91 (d, J=2.02 Hz, 1 H) 8.03 (d, J=8.59 Hz, 1 H)	475	20
I-615		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(1-methyl-1H-pyrazol-4-yl)-pyridin-2-ylamine		(400 MHz, CHLOROFORM-D) d ppm 1.84 (d, J=6.82 Hz, 3 H) 3.89 (s, 3 H) 4.79 (z, 2 H) 6.05 (q, J=6.57 Hz, 1 H) 6.94 (d, J=1.77 Hz, 1 H) 7.03 (m, 1 H) 7.28 (dd, J=8.97, 4.93 Hz, 1 H) 7.40 (s, 1 H) 7.53 (s, 1 H) 7.74 (d, J=1.77 Hz, 1 H)	381	19
I-616		(4-{6-Amino-5-[1-(2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(3,5-dimethyl-piperazin-1-yl)-methanone	3%	(400 MHz, DMSO-D6) d ppm 9.29 (d, J=9.60 Hz, 1 H) 8.63 (d, J=10.88 Hz, 1 H) 7.84 - 7.94 (m, 2 H) 7.72 (t, J=7.66 Hz, 3 H) 7.47 - 7.57 (m, 8 H) 7.35 (s, 1 H) 6.97 - 6.06 (m, 1 H) 3.37 (s, 2 H) 1.68 (d, J=6.06 Hz, 3 H) 1.15 (s, 6 H) 1.08 (s, 1 H)	500	33
I-617		(4-{6-Amino-5-[1-(3-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(3,5-dimethyl-piperazin-1-yl)-methanone	2%	(400 MHz, DMSO-D6) d ppm 9.29 (s, 2 H) 8.64 (s, 2 H) 7.93 (s, 2 H) 7.84 (d, J=1.52 Hz, 2 H) 7.81 (d, J=7.58 Hz, 2 H) 7.66 (s, 2 H) 7.60 (d, J=8.34 Hz, 5 H) 7.53 - 7.68 (m, 2 H) 7.48 (d, J=8.34 Hz, 4 H) 6.01 (q, J=6.32 Hz, 2 H) 3.22 (s, 4 H) 3.03 (s, 1 H) 2.75 (s, 1 H) 1.81 (d, J=6.32 Hz, 5 H) 1.13 (s, 7 H)	500	32
I-618		7-[4-(3,5-Dimethyl-piperazine-1-carbonyl)-phenyl]-3-phenyl-4H-pyrido[3,2-b][1,4]oxazin-3-one	0%	(400 MHz, DMSO-D6) d ppm 8.63 (s, 2 H) 8.33 (d, J=2.02 Hz, 2 H) 7.84 (d, J=2.02 Hz, 2 H) 7.80 (d, J=8.34 Hz, 5 H) 7.38 - 7.42 (m, 12 H) 5.93 (s, 2 H) 4.85 (s, 1 H) 3.73 (s, 3 H) 3.40 (s, 8 H) 1.18 (s, 10 H)	444	32

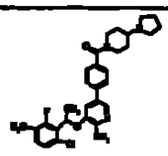
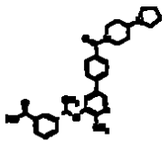
No.	Structure	Name	Ki (μM) or I (%)	^{1}H-NMR	MS m/z (M+H)	Procedure
I-619		[4-[5-Amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl]-(3,5-dimethyl-piperazin-1-yl)-methanone	16%	(400 MHz, DMSO-D6) d ppm 7.97 (d, J=1.77 Hz, 1 H) 7.78 (s, 1 H) 7.66 - 7.74 (m, 3 H) 7.48 (d, J=1.77 Hz, 2 H) 7.41 (d, J=8.34 Hz, 2 H) 7.24 (s, 1 H) 6.91 (s, 1 H) 5.40 (s, 2 H) 3.61 (s, 1 H) 2.81 - 2.70 (m, 3 H) 2.33 (s, 1 H) 2.17 (s, 1 H) 1.96 - 2.06 (m, 1 H) 1.47 (s, 1 H) 1.23 (s, 7 H) 1.00 (s, 3 H) 0.80 - 0.82 (m, 6 H)	504	32
I-620		[4-[5-Amino-6-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl]-(3,5-dimethyl-piperazin-1-yl)-methanone	8%	(400 MHz, DMSO-D6) d ppm 8.02 (s, 1 H) 7.86 (s, 1 H) 7.66 (d, J=8.34 Hz, 2 H) 7.51 - 7.62 (m, 3 H) 7.23 (t, J=8.08 Hz, 2 H) 5.43 (s, 2 H) 4.09 (s, 1 H) 3.37 (s, 1 H) 1.40 (s, 6 H) 1.14 (d, J=2.27 Hz, 3 H) 1.08 (d, J=16.42 Hz, 3 H)	464	34
I-621		[4-(5-Amino-6-benzyloxy-pyridin-3-yl)-phenyl]-(3,5-dimethyl-piperazin-1-yl)-methanone	6%	(400 MHz, DMSO-D6) d ppm 9.35 (s, 1 H) 8.70 (s, 1 H) 7.96 (s, 2 H) 7.76 (d, J=8.59 Hz, 4 H) 7.55 (d, J=8.08 Hz, 6 H) 7.42 (t, J=7.20 Hz, 2 H) 7.35 (t, J=7.33 Hz, 1 H) 5.40 (s, 2 H) 3.39 (s, 2 H) 3.16 (s, 1 H) 1.20 (s, 4 H)	416	34
I-622		[4-[5-Amino-6-[1-(3-chloro-2,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl]-(4-ethyl-piperazin-1-yl)-methanone	0.375	(400 MHz, DMSO-D6) d ppm 7.96 (d, J=1.77 Hz, 1 H) 7.87 (d, J=8.34 Hz, 2 H) 7.82 (s, 1 H) 7.46 (d, J=8.08 Hz, 3 H) 7.28 (d, J=1.77 Hz, 1 H) 6.11 (s, 1 H) 5.85 (s, 2 H) 3.82 (s, 1 H) 3.49 (s, 1 H) 2.44 (s, 2 H) 2.41 (d, J=7.07 Hz, 4 H) 1.85 (d, J=6.32 Hz, 3 H) 1.08 (t, J=7.20 Hz, 3 H)	502	4
I-623		[4-(5-Amino-6-benzyloxy-pyridin-3-yl)-phenyl]-(4-ethyl-piperazin-1-yl)-methanone	7%	(400 MHz, DMSO-D6) d ppm 7.91 (d, J=2.02 Hz, 1 H) 7.85 (d, J=8.34 Hz, 2 H) 7.53 (d, J=7.33 Hz, 2 H) 7.44 (d, J=1.77 Hz, 1 H) 7.37 - 7.42 (m, 3 H) 7.32 (t, J=7.33 Hz, 1 H) 5.34 (s, 2 H) 5.25 (s, 2 H) 3.60 (s, 1 H) 3.38 (s, 1 H) 2.30 - 2.41 (m, 6 H) 0.99 (t, J=7.20 Hz, 3 H)	418	34
I-624		[4-[5-Amino-6-(2-methyl-benzyloxy)-pyridin-3-yl]-phenyl]-(3,5-dimethyl-piperazin-1-yl)-methanone	0%	(400 MHz, DMSO-D6) d ppm 9.40 (s, 1 H) 8.77 (s, 1 H) 7.96 (d, J=1.52 Hz, 1 H) 7.77 - 7.85 (m, 4 H) 7.57 (d, J=8.34 Hz, 2 H) 7.53 (d, J=7.33 Hz, 1 H) 7.21 - 7.31 (m, 3 H) 5.37 (s, 2 H) 3.39 (s, 2 H) 2.37 (s, 3 H) 1.20 (s, 4 H)	432	34
I-625		3-[2-Amino-6-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl]-benzoic acid methyl ester	6%	(400 MHz, DMSO-D6) d ppm 9.75 (s, 1 H) 8.12 (s, 1 H) 7.92 - 7.96 (m, 2 H) 7.88 (d, J=7.58 Hz, 1 H) 7.74 - 7.83 (m, 3 H) 7.67 (t, J=7.71 Hz, 2 H) 7.46 (d, J=8.34 Hz, 2 H) 5.47 (s, 2 H) 3.89 (s, 3 H) 3.50 (s, 2 H) 3.41 (s, 1 H) 3.16 (s, 2 H) 2.00 (s, 3 H) 1.85 (s, 2 H) 1.65 (s, 2 H)	516	6
I-626		3-[2-Amino-6-[1-(3,5-dimethyl-piperazine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl]-benzoic acid methyl ester	0%	(400 MHz, DMSO-D6) d ppm 9.31 (s, 2 H) 8.67 (s, 2 H) 8.12 (s, 2 H) 7.92 - 7.99 (m, 4 H) 7.88 (d, J=7.83 Hz, 2 H) 7.73 - 7.84 (m, 6 H) 7.53 - 7.63 (m, 8 H) 5.48 (s, 4 H) 3.81 - 3.91 (m, 6 H) 3.39 (s, 4 H) 3.13 (s, 1 H) 1.20 (s, 7 H)	476	34
I-627		[4-[5-Amino-6-(2-methyl-benzyloxy)-pyridin-3-yl]-phenyl]-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	6%	(400 MHz, DMSO-D6) d ppm 9.91 (s, 1 H) 7.96 (d, J=1.52 Hz, 1 H) 7.88 (s, 1 H) 7.80 (d, J=8.34 Hz, 2 H) 7.53 (d, J=7.07 Hz, 1 H) 7.49 (d, J=8.34 Hz, 2 H) 7.21 - 7.31 (m, 3 H) 5.36 (s, 2 H) 4.56 (s, 1 H) 3.85 (s, 1 H) 3.61 (s, 2 H) 3.41 (s, 1 H) 3.10 (s, 3 H) 2.82 (s, 1 H) 2.37 (s, 3 H) 1.99 (s, 3 H) 1.79 - 1.90 (m, 2 H) 1.56 (s, 2 H)	472	6
I-628		[4-[5-Amino-6-cyclohexylmethoxy-pyridin-3-yl]-phenyl]-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	7%	(400 MHz, DMSO-D6) d ppm 7.90 (d, J=1.52 Hz, 1 H) 7.79 (d, J=8.34 Hz, 3 H) 7.66 (s, 1 H) 7.44 - 7.56 (m, 2 H) 4.03 (d, J=6.06 Hz, 2 H) 3.83 (s, 1 H) 3.67 (s, 1 H) 3.61 (s, 2 H) 3.39 (s, 1 H) 3.09 (s, 2 H) 2.82 (s, 1 H) 2.14 (s, 2 H) 1.99 (s, 3 H) 1.78 - 1.91 (m, 5 H) 1.64 - 1.76 (m, 3 H) 1.54 (s, 2 H) 1.20 - 1.30 (m, 2 H) 1.07 (d, J=11.62 Hz, 2 H)	464	6

No.	Structure	Name	Ki (μM) or I (%)	^{1}H-NMR	MS m/z (M+H)	Procedure
I-629		4-(1-[3-Amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxy]-ethyl)-[2-(3-hydroxy-phenyl)-ethyl]-benzamide	7%	(400 MHz, DMSO-D6) d ppm 9.76 (s, 1 H) 8.51 (t, J=6.66 Hz, 1 H) 7.88 (d, J=1.52 Hz, 2 H) 7.79 (d, J=8.34 Hz, 2 H) 7.63 (dd, J=14.40, 8.34 Hz, 5 H) 7.48 (d, J=8.34 Hz, 2 H) 7.04 (t, J=7.98 Hz, 1 H) 6.58 - 6.65 (m, 3 H) 6.00 (d, J=6.32 Hz, 1 H) 3.48 (s, 2 H) 3.34 - 3.45 (m, 3 H) 3.09 (s, 3 H) 2.75 (s, 1 H) 2.65 - 2.74 (m, 2 H) 2.13 (s, 1 H) 1.99 (s, 3 H) 1.78 - 1.89 (m, 2 H) 1.65 (d, J=6.32 Hz, 3 H) 1.52 (s, 2 H)	636	6
I-630		4-(1-[3-Amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxy]-ethyl)-[2-(2,6-dichloro-phenyl)-ethyl]-benzamide	3%	(400 MHz, DMSO-D6) d ppm 9.80 (s, 1 H) 8.62 (t, J=5.81 Hz, 1 H) 7.85 (d, J=1.26 Hz, 1 H) 7.78 (d, J=8.34 Hz, 3 H) 7.62 (dd, J=12.63, 8.34 Hz, 6 H) 7.39 - 7.49 (m, 4 H) 7.21 - 7.30 (m, 1 H) 5.98 (d, J=6.32 Hz, 1 H) 3.65 (s, 1 H) 3.40 - 3.61 (m, J=6.63, 6.63, 6.63, 6.63 Hz, 4 H) 3.03 - 3.15 (m, 5 H) 2.82 (s, 1 H) 2.13 (s, 1 H) 1.98 (s, 3 H) 1.78 - 1.89 (m, 2 H) 1.65 (d, J=6.06 Hz, 3 H) 1.53 (s, 2 H)	665	6
I-631		4-(1-[3-Amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxy]-ethyl)-(1-benzyl-piperidin-4-yl)-benzamide	3%	(400 MHz, DMSO-D6) d ppm 7.75 - 7.82 (m, 2 H) 7.58 - 7.67 (m, 4 H) 7.39 - 7.49 (m, 6 H) 4.27 (d, J=4.80 Hz, 2 H) 3.62 (s, 1 H) 3.49 (s, 2 H) 3.37 (s, 2 H) 3.07 (s, 3 H) 2.12 (s, 1 H) 1.82 - 2.04 (m, 4 H) 1.79 - 1.91 (m, 2 H) 1.71 (d, J=11.87 Hz, 1 H) 1.59 - 1.68 (m, 3 H) 1.51 (s, 2 H)	684	4
I-632		4-(1-[3-Amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxy]-ethyl)-[3-(2-oxo-pyrrolidin-1-yl)-propyl]-benzamide	0%	(400 MHz, DMSO-D6) d ppm 8.39 (s, 1 H) 7.77 - 7.85 (m, 3 H) 7.61 (t, J=8.08 Hz, 5 H) 7.43 (d, J=8.34 Hz, 2 H) 5.98 (s, 1 H) 3.69 (s, 2 H) 3.49 (s, 3 H) 3.36 (s, 2 H) 3.30 (t, J=6.95 Hz, 3 H) 3.14 - 3.22 (m, 4 H) 3.09 (s, 3 H) 2.18 (t, J=8.08 Hz, 2 H) 2.00 (s, 3 H) 1.88 (ddd, J=15.28, 7.59, 7.48 Hz, 4 H) 1.65 (t, J=6.06 Hz, 5 H) 1.52 (s, 2 H)	640	6
I-633		(1-[5-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-ethyl-piperazin-1-yl)-methanone	0.0472	(400 MHz, DMSO-D6) d ppm 9.85 (s, 1 H) 7.91 (d, J=1.77 Hz, 1 H) 7.56 (dd, J=2.67, 1.93 Hz, 1 H) 7.50 - 7.55 (m, 4 H) 7.44 - 7.50 (m, 1 H) 7.13 (d, J=1.52 Hz, 1 H) 6.27 (q, J=6.57 Hz, 1 H) 3.48 (s, 2 H) 3.15 (q, J=7.07 Hz, 3 H) 3.08 (s, 2 H) 1.94 (d, J=6.57 Hz, 3 H) 1.22 (t, J=7.33 Hz, 3 H)	518	6
I-634		(1-[5-Amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl)-(3,5-dimethyl-piperazin-1-yl)-methanone	10%	(400 MHz, DMSO-D6) d ppm 9.29 (s, 2 H) 8.99 (s, 2 H) 7.91 - 8.00 (m, 5 H) 7.85 (d, J=6.82 Hz, 5 H) 7.54 - 7.61 (m, 10 H) 7.49 - 7.53 (m, 3 H) 5.46 (s, 5 H) 4.61 (s, 1 H) 1.21 (d, J=4.55 Hz, 9 H) 1.16 (s, 5 H)	466	31
I-635		(5-Amino-3-aza-bicyclo[3.1.0]hex-3-yl)-(4-[5-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-methanone	0.0554	(400 MHz, DMSO-D6) d ppm 8.14 (d, J=3.54 Hz, 3 H) 7.87 (s, 1 H) 7.58 (dd, J=8.97, 4.93 Hz, 1 H) 7.44 - 7.53 (m, 5 H) 7.12 (s, 1 H) 6.25 (s, 1 H) 3.98 (d, J=11.87 Hz, 1 H) 3.69 (s, 2 H) 1.96 (d, J=13.39 Hz, 2 H) 1.84 (d, J=6.57 Hz, 3 H)	502	35
I-636		5-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5'-(2-morpholin-4-yl-ethoxy)-[3,3']bipyridinyl-6-ylamine	0.109	(400 MHz, DMSO-D6) d ppm 8.30 (d, J=2.27 Hz, 1 H) 7.83 (d, J=1.77 Hz, 1 H) 7.79 (dd, J=8.59, 2.53 Hz, 1 H) 7.61 (dd, J=8.97, 4.93 Hz, 1 H) 7.49 (t, J=8.84 Hz, 1 H) 6.89 (d, J=1.77 Hz, 1 H) 6.69 (d, J=8.59 Hz, 1 H) 6.19 (q, J=6.82 Hz, 1 H) 5.92 (s, 2 H) 4.41 (t, J=5.81 Hz, 2 H) 3.61 (m, 4 H) 2.72 (t, J=5.81 Hz, 2 H) 2.47 - 2.52 (m, 4 H) 1.85 (d, J=6.57 Hz, 3 H)	507	38
I-637		6'-Amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-1-(2-pyrrolidin-1-yl-ethyl)-1H-[3,3']bipyridinyl-6-one	0.882	(400 MHz, DMSO-D6) d ppm 7.42 - 7.52 (m, 2 H) 7.25 - 7.35 (m, 2 H) 7.22 (t, J=8.72 Hz, 1 H) 6.64 (d, J=1.52 Hz, 1 H) 6.19 (d, J=6.35 Hz, 1 H) 6.09 (q, J=6.74 Hz, 1 H) 5.88 (s, 2 H) 3.72 - 3.84 (m, 2 H) 2.42 - 2.53 (m, 2 H) 1.57 (d, J=6.57 Hz, 3 H) 1.39 - 1.50 (m, 4 H)	491	35

No.	Structure	Name	K_i (μM) or	(%)	^{1}H-NMR	MS m/z (M+H)	Procedure
I-638		6-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5'-(3-pyrrolidin-1-yl-ethoxy)-[3,3']bipyridinyl-6-ylamine	0.094		(400 MHz, DMSO-D6) d ppm 7.98 (d, J=2.53 Hz, 1 H) 7.82 (d, J=2.02 Hz, 1 H) 7.57 (dd, J=8.59, 2.53 Hz, 1 H) 7.40 (dd, J=8.97, 4.93 Hz, 1 H) 7.27 (t, J=8.72 Hz, 1 H) 6.77 (d, J=1.77 Hz, 1 H) 6.68 (d, J=8.59 Hz, 1 H) 6.57 (q, J=8.67 Hz, 1 H) 5.70 (s, 2 H) 4.17 (t, J=5.81 Hz, 2 H) 2.58 - 2.65 (m, 2 H) 1.83 (d, J=8.82 Hz, 3 H) 1.48 - 1.64 (m, 4 H) 0.87 - 1.09 (m, 1 H)	491	35
I-639		6'-Amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-1-[2-(1-methyl-pyrrolidin-3-yl)-ethyl]-1H-[3,3']bipyridinyl-6-one	0.513		(400 MHz, DMSO-D6) d ppm 7.71 (dd, J=8.60, 1.77 Hz, 2 H) 7.46 - 7.56 (m, 2 H) 7.42 (t, J=8.72 Hz, 1 H) 6.84 (s, 1 H) 6.39 (d, J=8.35 Hz, 1 H) 6.10 (q, J=6.57 Hz, 1 H) 5.79 (s, 2 H) 3.98 - 4.08 (m, 4 H) 3.81 - 3.92 (m, 2 H) 2.85 - 2.92 (m, 2 H) 2.14 - 2.18 (m, 7 H) 1.93 - 2.05 (m, 5 H) 1.84 - 1.89 (m, 2 H) 1.76 - 1.82 (m, 4 H) 1.62 - 1.63 (m, 6 H) 1.26 - 1.36 (m, 2 H) 1.06 - 1.16 (m, 6 H)	503	3
I-640		(4-{6-Amino-5-[1-(2,4,6-trimethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone			(400 MHz, MeOD) d ppm 7.62 (d, J=1.52 Hz, 1 H) 7.25 - 7.31 (m, 2 H) 7.19 - 7.25 (m, 2 H) 6.73 (s, 2 H) 6.65 (d, J=1.77 Hz, 1 H) 6.55 (q, J=6.57 Hz, 1 H) 4.46 - 4.57 (m, 1 H) 3.81 - 3.73 (m, 1 H) 2.96 - 3.07 (m, 1 H) 2.73 - 2.84 (m, 1 H) 2.50 - 2.59 (m, 4 H) 2.23 - 2.31 (m, 7 H) 2.10 (s, 3 H) 1.92 - 2.04 (m, 1 H) 1.77 - 1.86 (m, 1 H) 1.69 - 1.76 (m, 4 H) 1.65 (d, J=6.82 Hz, 3 H) 1.29 - 1.40 (m, 2 H)	513	6
I-641		(4-{6-Amino-5-[1-(2-chloro-6-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone			(400 MHz, MeOD) d ppm 7.66 (d, J=2.02 Hz, 1 H) 7.25 - 7.39 (m, 4 H) 7.12 - 7.23 (m, 2 H) 7.07 (d, J=1.77 Hz, 1 H) 6.92 - 7.02 (m, 1 H) 6.67 (q, J=6.65 Hz, 1 H) 4.44 - 4.56 (m, 1 H) 3.62 - 3.74 (m, 1 H) 2.96 - 3.09 (m, 1 H) 2.72 - 2.84 (m, 1 H) 2.48 - 2.59 (m, 4 H) 2.20 - 2.31 (m, 1 H) 1.91 - 2.02 (m, 1 H) 1.78 - 1.89 (m, 1 H) 1.66 - 1.77 (m, 8 H) 1.28 - 1.40 (m, 2 H)	523	6
I-642		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(4-fluoro-phenyl)-pyridin-2-ylamine			(400 MHz, DMSO-D6) d ppm 7.81 (d, J=1.77 Hz, 1 H) 7.38 (dd, J=8.97, 4.93 Hz, 1 H) 7.30 - 7.28 (m, 3 H) 6.99 - 7.07 (m, 2 H) 6.78 (d, J=1.77 Hz, 1 H) 6.65 (q, J=6.65 Hz, 1 H) 6.70 (s, 2 H) 1.82 (d, J=6.57 Hz, 3 H)	395	1
I-643		6'-Amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-1H-[3,3']bipyridinyl-6-one	0.0432		(500 MHz, DMSO-D6) d ppm 7.73 (s, 1 H) 7.73-7.46 (m, 5 H) 7.09 (d, J=1.55 Hz, 1 H) 6.42 (d, J=9.5 Hz, 1 H) 6.22 (q, J=6.65 Hz, 1 H) 1.84 (d, J=6.60 Hz, 3 H)	394	3
I-644		5'-Bromo-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6-ylamine	0.1968		(300 MHz, CDCl3-D1) d ppm 8.64 (d, 2 H) 7.80 (m, 2 H) 7.33 (m, 1 H) 7.09 (m, 1 H) 6.93 (s, 1 H) 6.12 (q, J = 6.7 Hz, 1 H) 5.041 (br. s, 2 H) 1.89 (d, J = 6.7 Hz, 3 H)	458 [M+2]	3
I-645		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(4-dimethylamino-phenyl)-pyridin-2-ylamine	0.1572		(300 MHz, CDCl3-D1) d ppm 7.83 (d, J = 1.67 Hz, 1 H) 7.28 (m, 4 H) 7.04 (m, 1 H) 6.89 (d ,J = 1.76 Hz , 1 H) 6.75 (m, 2 H) 6.11 (q, J = 6.7 Hz, 1 H) 4.76 (br. s, 2 H) 2.97 (s, 6 H) 1.85 (d, J = 6.7 Hz, 3 H)	420	3
I-646		5-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-3'-methoxy-[3,3']bipyridinyl-6-ylamine	0.099		(300 MHz, CDCl3-D1) d ppm 8.10 (s, 1 H) 7.77 (s, 1 H) 7.50 (m, 1 H) 7.30 (m, 1 H) 7.09 (m, 2 H) 6.92 (m, 1 H) 6.06 (d, J = 6.7 Hz, 1 H) 4.91 (br. s, 2 H) 3.87 (s, 3 H) 1.83 (d, J = 6.7 Hz, 3 H)	MS 408 m/z	3
I-647		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(1H-indol-5-yl)-pyridin-2-ylamine	0.1694		(300 MHz, CDCl3-D1) d ppm 8.21 (s, 1 H) 7.93 (m, 1 H) 7.84 (m, 1 H) 7.43 (m, 1 H) 7.32-7.21 (m, 3 H) 7.09-7.024 (m, 2 H) 6.66 (m, 1 H) 6.16 (m, 1 H) 4.80 (s, 2 H) 3.80 (s, 2 H) 1.87 (d, J=6.69 Hz, 3 H)	416	3
I-648		(4-{6-Amino-5-[1-(2,6-dichloro-phenyl)-propoxy]-pyridin-3-yl}-phenyl)-(3,5-dimethyl-piperazin-1-yl)-methanone	0.5833		(300 MHz, CDCl3-D1) d ppm 7.87 (s, 1 H) 7.42 (m, 4 H) 7.30 (m, 3 H) 7.16 (m, 1 H) 7.05 (s, 1 H) 5.92 (m, 1 H) 4.97 (s, 2 H) 4.61 (br. s, 1 H) 3.85 (br. s, 2 H) 2.85 (br. s, 3 H) 2.49 (br. s, 1 H) 2.41 (m, 3 H) 2.19 (m, 1 H) 1.06 (m, 6 H)	513	1

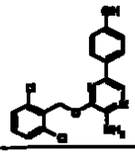
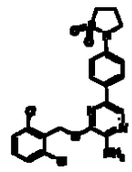
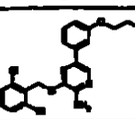
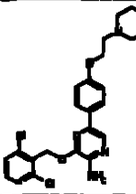
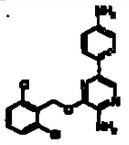
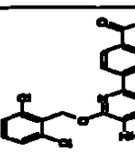
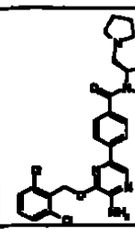
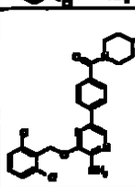
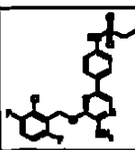
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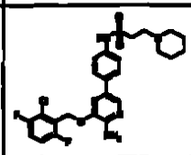
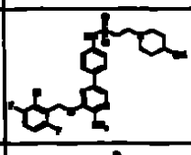
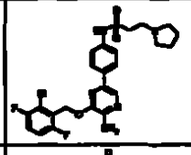
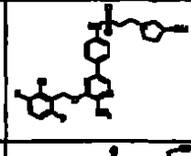
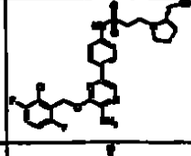
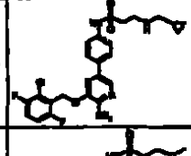
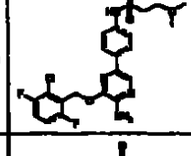
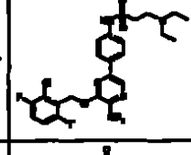
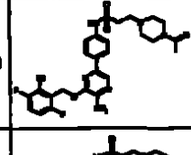
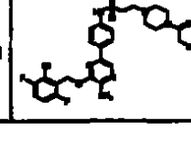
No.	Structure	Name	IC (μM) or I (%)	^{1}H-NMR	MS m/z (M+H)	Procedure
I-649		(4-[5-Amino-6-benzyloxy-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	20%	(400 MHz, DMSO-D6) d ppm 7.92 (d, J=1.77 Hz, 1 H) 7.89 (d, J=8.34 Hz, 2 H) 7.83 (d, J=7.07 Hz, 2 H) 7.37 - 7.48 (m, 5 H) 7.33 (m, 1 H) 6.96 (s, 2 H) 5.28 (s, 2 H) 3.49 (s, 2 H) 3.09 (s, 2 H) 2.09 (s, 2 H) 1.84 (s, 2 H) 1.56 (s, 1 H)	457	1
I-650		3-(2,6-Dichloro-3-fluoro-benzyloxy)-5-thiazol-2-yl-pyridin-2-ylamine	0.3627	(300 MHz, CDCl3-D1) d ppm 8.28 (d, J = 1.79 Hz, 1 H) 7.76 (d, J = 3.30 Hz) 7.36-7.26 (m, 3 H) 7.20 (m , 1 H) 7.05 (m, 1H) 6.17 (q, J = 6.7 Hz, 1 H) 5.09 (br. s, 2 H) 1.86 (d, J = 6.7 Hz, 3 H)	384	37
I-651		(4-[5-Amino-6-[1-(2-fluoro-6-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	1.5258	(400 MHz, DMSO-D6) d ppm 7.93 (d, J=1.52 Hz, 1 H) 7.74 - 7.82 (m, 3 H) 7.71 m, 3 H) 7.62 - 7.67 (m, 3 H) 7.47 (m, 4 H) 7.38 (m, 1 H) 5.43 (s, 2 H) 3.67 (br. s, 2 H) 3.51 (br. s, 3 H) 3.40 (br. s, 1 H) 3.09 (br. s, 2 H) 2.00 (br. s, 3 H) 1.83 (br. s, 2 H) 1.53 (br. s, 2 H)	633	6
I-652		3-(2,6-Dichloro-3-fluoro-benzyloxy)-5-(1-methyl-1H-imidazol-2-yl)-pyridin-3-ylamine	11%	(300 MHz, CDCl3-D1) d ppm 7.90 (d, J = 1.67 Hz, 1 H) 7.30 (m, 2H) 7.05 (m, 3 H) 6.91 (d, J = 0.98 Hz, 1 H) 6.10 (q, J = 6.7 Hz, 1 H) 4.99 (br. s, 2 H) 3.57 (s, 3 H) 1.83 (d, J = 6.7 Hz, 3 H)	381	38
I-653		(4-[5-Amino-6-(2,4,6-trimethyl-benzyloxy)-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	2%	(400 MHz, DMSO-D6) d ppm 7.92 (s, 1 H) 7.90 (s, 1 H) 7.84 (d, J=8.34 Hz, 2 H) 7.80 (d, J=8.34 Hz, 2 H) 6.92 (s, 2 H) 6.27 (s, 2 H) 3.51 (br. s, 6 H) 3.09 (br. s, 3 H) 2.32 (s, 6 H) 2.25 (s, 3 H) 1.99 (br. s, 2 H) 1.84 (br. s, 2 H) 1.58 (br. s, 2 H)	499	6
I-654		(4-[5-Amino-6-(2,3,5,6-tetramethyl-benzyloxy)-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	9%	(400 MHz, DMSO-D6) d ppm 9.75 (s, 1 H) 7.88 (s, 2 H) 7.79 (d, J=8.34 Hz, 2 H) 7.45 (d, J=8.08 Hz, 3 H) 6.87 (s, 1 H) 5.28 (c, 2 H) 3.84 (s, 1 H) 3.46 (c, 2 H) 3.34 (s, 1 H) 3.04 (t, 3 H) 2.15 (s, 12 H) 1.94 (s, 3 H) 1.79 (c, 2 H) 1.60 (s, 2 H)	513	6
I-655		(4-[5-Amino-6-(2,4,6-trifluoro-benzyloxy)-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone		(400 MHz, DMSO-D6) d ppm 7.83 (d, J=2.02 Hz, 1 H) 7.48 (d, J=8.34 Hz, 3 H) 7.33 (d, J=8.34 Hz, 3 H) 7.24 (d, J=1.77 Hz, 1 H) 7.12 - 7.22 (m, 2 H) 6.86 (m, 1 H) 6.76 (s, 2 H) 4.19 (br. s, 1 H) 3.55 (br. s, 1 H) 2.86 (br. s, 2 H) 2.16 (br. s, 1 H) 1.83 (br. s, 2 H) 1.69 (br. s, 6 H) 1.60 (d, J= 5.87 Hz, 5 H) 1.30 (br. s, 2 H)	625	6
I-656		(4-[5-Amino-6-[1-(2-fluoro-6-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone		(400 MHz, DMSO-D6) d ppm 7.92 (d, J=1.77 Hz, 1 H) 7.87 - 7.68 (m, 3 H) 7.41 - 7.49 (m, 2 H) 7.36 (d, J=8.08 Hz, 2 H) 7.19 (d, J=1.77 Hz, 1 H) 6.85 (s, 2 H) 5.80 (s, 1 H) 4.21 (s, 1 H) 3.57 (br. s, 1H) 3.02 (s, 2 H) 2.22 (s, 1 H) 1.80 (br. s, 2H) 1.76 (d, J=6.3 Hz, 3 H) 1.69 (s, 4 H) 1.34 (s, 2 H)	557	6
I-657		6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-N-methyl-nicotinamidine		(400 MHz, DMSO-D6) δ ppm 8.82 (br. s, 1 H) 7.97 (d, J=1.77 Hz, 1 H) 7.82 - 7.87 (m, 1 H) 7.48 (t, J=8.72 Hz, 1 H) 7.08 (d, J=1.26 Hz, 1 H) 6.73 (br. s, 1 H) 6.09 (quart., J=6.57 Hz, 1 H) 2.91 (s, 3 H) 1.78 (d, J=6.57 Hz, 3 H)	357	39
I-658		6-Amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-N-(3-morpholin-4-yl-ethyl)-nicotinamidine		(400 MHz, DMSO-D6) δ ppm 9.07 (br. s, 1 H) 7.94 (d, J=1.52 Hz, 1 H) 7.53 (m, 1 H) 7.47 (m, 1 H) 6.97 (s, 1 H) 6.77 (br. s, 1 H) 6.09 (s, 1 H) 3.55 (quart, J=4.29 Hz, 2 H) 3.54 (m, 2 H) 3.47 (m, 2 H) 2.54 (t, J=6.06 Hz, 2 H) 2.42 (s, 3 H) 1.78 (d, J=6.82 Hz, 3 H)	456	39
I-659		(4-[5-Amino-6-[1-(2,4,5-trifluoro-phenyl)-propoxy]-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone		(400 MHz, DMSO-D6) d ppm 9.84 (s, 1 H) 7.91 (d, J=1.52 Hz, 1 H) 7.78 - 7.88 (m, 1 H) 7.65 - 7.76 (m, 3 H) 7.57 (dd, J=10.23, 3.66 Hz, 1 H) 7.46 (d, J=8.34 Hz, 2 H) 5.91 - 5.99 (m, 1 H) 3.50 (s, 2 H) 3.40 (s, 1 H) 3.09 (s, 2 H) 2.09 (dt, J=14.08, 6.98 Hz, 2 H) 1.98 (s, 2 H) 1.82 (dt, J=13.90, 6.95 Hz, 2 H) 1.63 (s, 2 H) 1.56 (s, 2 H) 0.92 (t, J=7.33 Hz, 3 H)	540	6

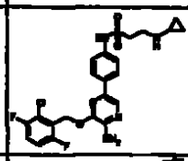
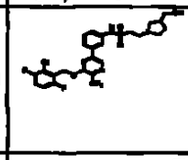
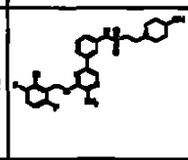
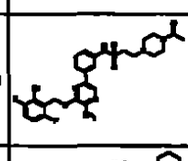
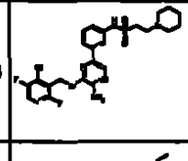
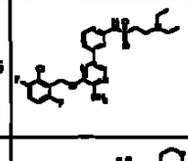
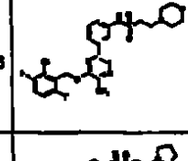
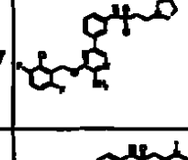
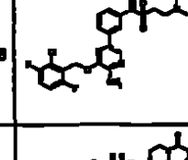
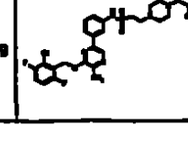
No.	Structure	Name	Ki (μM) or I (%)	^{1}H-NMR	MS m/z (M+H)	Procedure
I-660		(4-{6-Amino-5-[1-(3-chloro-2-fluoro-3-methyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone		NMR (400 MHz, DMSO-D6) d ppm 9.84 (s, 1 H) 7.95 (s, 2 H) 7.85 (d, J=8.34 Hz, 2 H) 7.83 - 7.80 (m, 2 H) 7.48 (s, 1 H) 7.32 - 7.42 (m, 2 H) 6.25 (q, J=6.48 Hz, 1 H) 3.88 (s, 2 H) 3.49 (s, 1 H) 3.18 (d, J=5.08 Hz, 3 H) 2.27 (d, J=1.82 Hz, 5 H) 2.01 - 2.13 (m, 4 H) 1.89 (d, J=6.57 Hz, 5 H) 1.64 (s, 2 H)	539	6
I-661		3-(1-{2-Amino-6-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxy}-ethyl)-benzoic acid		(400 MHz, DMSO-D6) d ppm 10.14 (s, 1 H) 8.12 (s, 1 H) 7.93 (s, 1 H) 7.78 - 7.87 (m, 4 H) 7.72 (s, 1 H) 7.65 (d, J=8.34 Hz, 2 H) 7.53 (ddd, J=15.92, 7.83, 7.58 Hz, 2 H) 7.40 - 7.47 (m, 3 H) 6.03 - 6.10 (m, 1 H) 4.55 (s, 1 H) 3.84 (s, 1 H) 3.47 (s, 2 H) 3.38 (s, 1 H) 3.07 (s, 3 H) 2.13 (s, 1 H) 1.95 (s, 3 H) 1.75 - 1.89 (m, 3 H) 1.65 (t, J=6.69 Hz, 3 H) 1.56 (s, 2 H) 1.31 (d, J=6.57 Hz, 2 H)	515	6

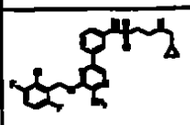
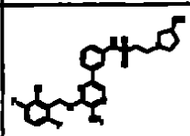
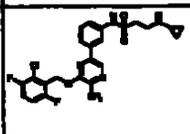
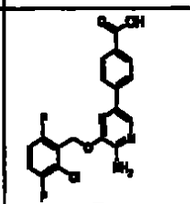
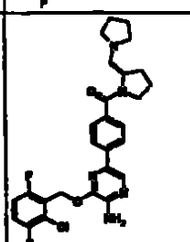
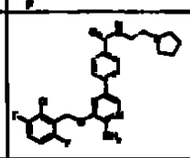
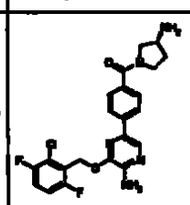
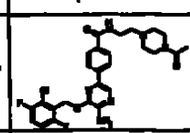
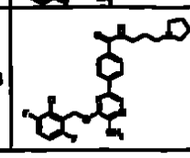
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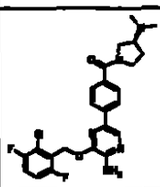
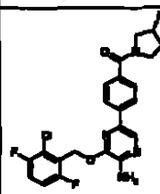
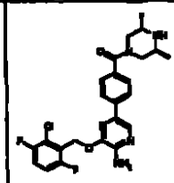
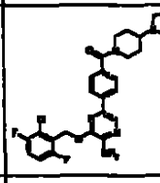
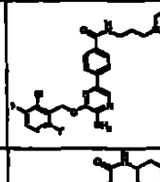
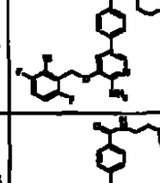
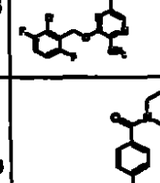
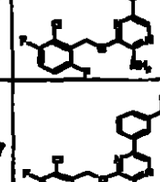
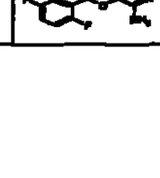
Table 4

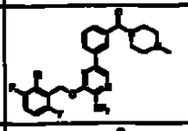
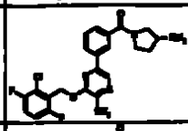
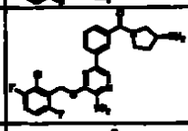
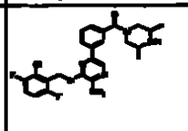
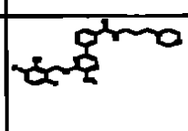
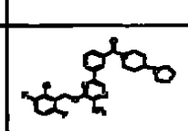
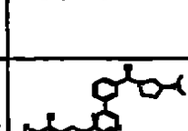
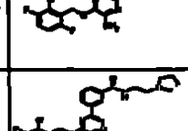
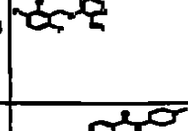
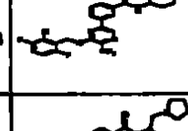
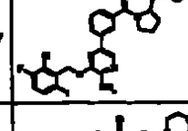
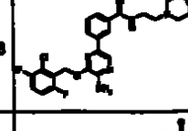
No.	Structure	Name	Mast IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-1		4-[5-Amino-6-(2,6-dichloro-benzyloxy)-pyrazin-2-yl]-phenol	1.36	see examples	(400 MHz, DMSO-d_6) δ 5.61 (s, 2H), 6.09 (s, 2H), 6.79 (d, 2H), 7.45 (t, 1H), 7.56 (d, 2H), 7.76 (d, 2H), 7.99 (s, 1H), 9.48 (s, 1H)	362
II-2		3-(2,6-Dichloro-benzyloxy)-5-[4-(1,1-dioxo-12^6-isothiazolidin-2-yl)-phenyl]-pyrazin-2-ylamine	0.825	see examples	(400 MHz, DMSO-d_6) δ 2.41 (m, 2H), 3.61 (m, 2H), 3.76 (m, 2H), 5.62 (s, 2H), 6.28 (s, 2H), 7.22 (m, 2H), 7.48 (m, 1H), 7.58 (m, 2H), 7.94 (m, 2H), 8.14 (s, 1H)	465
II-3		3-(2,6-Dichloro-benzyloxy)-5-[3-(2-morpholin-4-yl-ethoxy)-phenyl]-pyrazin-2-ylamine	0.74	see examples	(400MHz, DMSO-d_6) δ 2.48 (m, 4H), 2.71 (t, 2H), 3.58 (t, 4H), 4.16 (t, 2H), 5.61 (s, 2H), 6.32 (s, 2H), 6.86 (d, 1H), 7.29 (t, 1H), 7.46 (m, 2H), 7.52 (m, 1H), 7.56 (s, 1H), 7.57 (d, 1H), 8.19 (s, 1H)	476
II-4		3-(2,6-Dichloro-benzyloxy)-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyrazin-2-ylamine	1.25	see examples	(400 MHz, DMSO-d_6) δ 2.46 (m, 4H), 2.71 (m, 2H), 3.59 (t, 4H), 4.11 (t, 2H), 5.64 (s, 2H), 6.18 (s, 2H), 6.97 (d, 2H), 7.48 (t, 1H), 7.56 (d, 2H), 7.96 (d, 2H), 8.08 (s, 1H)	475
II-5		5-(4-Amino-phenyl)-3-(2,6-dichloro-benzyloxy)-pyrazin-2-ylamine	0.94	see examples	(400 MHz, DMSO-d_6) δ 5.19 (s, 2H), 5.59 (s, 2H), 5.96 (s, 2H), 6.60 (d, 2H), 7.45 (t, 1H), 7.56 (d, 2H), 7.82 (d, 2H), 7.91 (s, 1H)	361
II-6		4-[5-Amino-6-(2,6-dichloro-benzyloxy)-pyrazin-2-yl]-benzoic acid	1.75	see examples	(400 MHz, DMSO-d_6) δ 5.84 (s, 2H), 6.62 (s, 2H), 7.46 (m, 1H), 7.56 (m, 2H), 7.96 (d, 2H), 8.07 (d, 2H), 8.57 (s, 1H)	390
II-7		{4-[5-Amino-6-(2,6-dichloro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(2R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.24	see examples	(400 MHz, DMSO-d_6) δ 1.79 (m, 10H), 2.64 (m, 4H), 3.48 (m, 3H), 5.64 (s, 2H), 6.42 (s, 2H), 7.49 (m, 3H), 7.58 (m, 2H), 7.98 (d, 2H), 8.00 (s, 1H)	539
II-8		{4-[5-Amino-6-(2,6-dichloro-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.56	see examples	(400 MHz, DMSO-d_6) δ 1.37 (m, 2H), 1.66 (m, 4H), 1.85 (m, 2H), 2.32 (m, 2H), 2.52 (m, 4H), 3.04 (m, 2H), 3.92 (m, 1H), 5.62 (s, 2H), 6.42 (s, 2H), 7.40 (d, 2H), 7.48 (t, 1H), 7.58 (m, 2H), 8.00 (d, 2H), 8.21 (s, 1H)	539
II-9		2-Morpholin-4-yl-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide	1.26	see examples	(300 MHz, $CDCl_3$) δ 2.50 (t, 4H), 2.62 (t, 2H), 3.29 (t,2H), 3.72 (t, 2H), 4.61 (s, 2H), 5.67 (d, 2H), 7.06 (m, 1H), 7.20 (m, 1H), 7.28 (d, 2H), 7.90 (d, 2H), 8.04 (s, 1H)	640

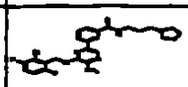
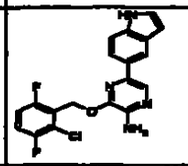
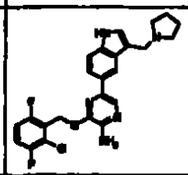
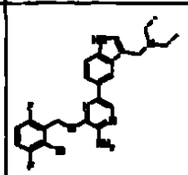
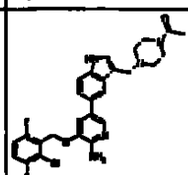
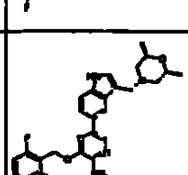
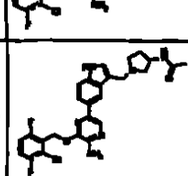
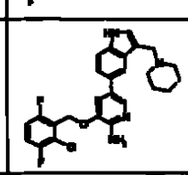
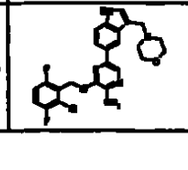
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-10		2-Piperidin-1-yl-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide	1.2	see examples	(300 MHz, $CDCl_3$) δ 1.50 (m, 2H), 1.63 (m, 4H), 2.48 (m, 4H), 2.90 (t, 2H), 3.28 (t, 2H), 4.85 (s, 2H), 5.67 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.29 (d, 2H), 7.89 (d, 2H), 8.04 (s, 1H)	638
II-11		2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide	0.85	see examples	(300 MHz, $CDCl_3$) δ 1.63 (m, 2H), 1.90 (m, 2H), 2.27 (t, 2H), 2.80 (m, 2H), 2.82 (t, 2H), 4.86 (s, 2H), 5.67 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.29 (d, 2H), 7.89 (d, 2H), 8.04 (s, 1H)	654
II-12		2-Pyrrolidin-1-yl-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide	0.88	see examples	(300 MHz, $CDCl_3$) δ 1.83 (m, 4H), 2.68 (m, 4H), 3.04 (t, 2H), 3.38 (t, 2H), 4.91 (s, 2H), 5.67 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.27 (d, 2H), 7.89 (d, 2H), 8.03 (s, 1H)	624
II-13		2-[(3R)-3-Hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide	1.58	see examples	(300 MHz, $CDCl_3$) δ 1.85 (m, 1H), 2.25 (m, 2H), 2.55 (m, 1H), 2.84 (d, 1H), 3.02 (m, 3H), 3.26 (m, 2H), 4.43 (m, 1H), 4.82 (s, 2H), 5.67 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.35 (d, 2H), 7.89 (d, 2H), 8.04 (s, 1H)	640
II-14		2-[(2S)-2-Hydroxymethyl-pyrrolidin-1-yl]-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide	1.78	see examples	(300 MHz, $CDCl_3$) δ 1.85 (m, 4H), 2.20 (m, 1H), 2.70 (m, 2H), 3.05 (m, 2H), 3.30-3.70(m, 3H), 3.95 (m, 1H), 4.78 (s, 2H), 5.67 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.32 (d, 2H), 7.89 (d, 2H), 8.05 (s, 1H)	654
II-15		2-(Cyclopropylmethyl-amino)-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide	1.29	see examples	^{1}H NMR (300 MHz, $CDCl_3$) δ 0.14 (m, 2H), 0.52 (m, 2H), 0.95 (m, 1H), 2.60 (d, 2H), 3.21(m, 4H), 4.86 (s, 2H), 5.67 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.30 (d, 2H), 7.89 (d, 2H), 8.04 (s, 1H)	634
II-16		2-Dimethylamino-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide	0.91	see examples	(300 MHz, $CDCl_3$) δ 2.30 (s, 6H), 2.95 (t, 2H), 3.21 (t, 2H), 4.83 (s, 2H), 5.67 (d, 2H), 7.05 (m, 1H), 7.19 (m, 1H), 7.28 (d, 2H), 7.89 (d, 2H), 8.05 (s, 1H)	495
II-17		2-Diethylamino-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide	0.48	see examples	(300 MHz, $CDCl_3$) δ 1.06 (t, 6H), 2.61 (q, 4H), 3.03 (t, 2H), 3.23 (t, 2H), 4.80 (s, 2H), 5.67 (d, 2H), 7.02 (m, 1H), 7.19 (m, 1H), 7.27 (d, 2H), 7.88 (d, 2H), 8.04 (s, 1H)	526
II-18		2-(4-Acetyl-piperazin-1-yl)-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide	1.5	see examples	(300 MHz, $CDCl_3$) δ 2.06 (s, 3H), 2.48 (m, 4H), 2.93 (t, 2H), 3.30 (t, 2H), 3.47 (t, 2H), 3.62 (t, 2H), 4.82 (s, 2H), 5.67 (s, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.29 (d, 2H), 7.91 (d, 2H), 8.05 (s, 1H)	651
II-19		2-[4-(2-Hydroxy-acetyl)-piperazin-1-yl]-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide	0.45	see examples	(300 MHz, $CDCl_3$) δ 2.48 (t, 4H), 2.83 (t, 2H), 3.30 (m, 4H), 3.55 (bra, 1H), 3.67 (t, 2H), 4.14 (s, 2H), 4.84 (s, 2H), 5.67 (s, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.27 (d, 2H), 7.92 (d, 2H), 8.05 (s, 1H)	667

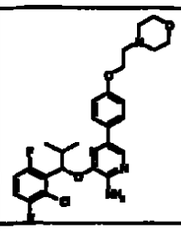
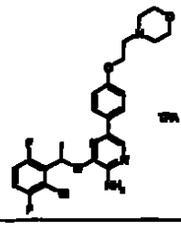
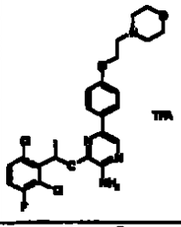
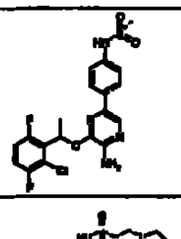
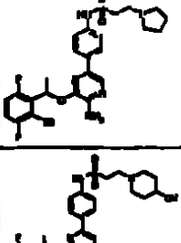
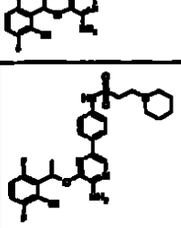
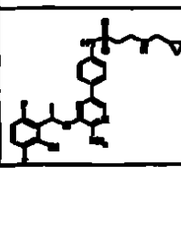
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-20		2-Cyclopropylamino-ethanesulfonic acid [4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl]-amide	1.29	see examples	(300 MHz, $CDCl_3$) δ 0.37 (m, 2H), 0.49 (m, 2H), 2.14 (m, 1H), 3.24 (m, 4H), 4.93 (s, 2H), 5.57 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.28 (d, 2H), 7.90 (d, 2H), 8.03 (s, 1H)	610
II-21		2-[(3R)-3-Hydroxymethyl-pyrrolidin-1-yl]-ethanesulfonic acid [3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl]-amide	1.38	see examples	(300 MHz, $CDCl_3$) δ 1.60-2.0 (m, 6H), 2.15 (m, 1H), 2.55-2.70 (m, 2H), 2.90-3.15 (m, 2H), 3.3-3.62 (m, 2H), 3.69 (dd, J = 3.0, 11.3 Hz, 1H), 4.82 (s, 2H), 5.66 (s, 2H), 6.95-7.60 (m, 6H), 7.55-7.70 (m, 2H), 7.77 (s, 1H), 8.10 (s, 1H)	554
II-22		2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid [3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl]-amide	0.7	see examples	(300 MHz, $CDCl_3$) δ 1.40-1.60 (m, 2H), 1.75-1.88 (m, 2H), 2.21 (t, J = 9.0 Hz, 2H), 2.68-2.75 (m, 2H), 2.85-2.98 (m, 2H), 3.20-3.35 (m, 2H), 3.69 (m, 1H), 5.17 (s, 2H), 5.66 (s, 2H), 6.92-7.02 (m, 1H), 7.05-7.20 (m, 1H), 7.30-7.45 (m, 2H), 7.69 (s, 1H), 7.76 (d, J = 7.5 Hz, 1 H), 8.14 (s, 1H)	656
II-23		2-(4-Acetyl-piperazin-1-yl)-ethanesulfonic acid [3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl]-amide	2.79	see examples	(300 MHz, $CDCl_3$) δ 2.03 (s, 3H), 2.30-2.40 (m, 2H), 2.75-2.85 (m, 2H), 3.20-3.40 (m, 4H), 3.45-3.66 (m, 2H), 5.35 (s, 2H), 5.66 (s, 2H), 6.95-7.02 (m, 1H), 7.05-7.20 (m, 1H), 7.30-7.45 (m, 2H), 7.64 (s, 1H), 7.76 (d, J = 7.5 Hz, 1H), 8.13 (s, 1H), 8.52 (s, 1H)	682
II-24		2-Piperidin-1-yl-ethanesulfonic acid [3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl]-amide	3.8	see examples	(300 MHz, $CDCl_3$) δ 1.30-1.60 (m, 6H), 2.30-2.45 (m, 4H), 2.75-2.90 (m, 2H), 3.15-3.30 (m, 2H), 5.10 (s, 2H), 5.66 (s, 2H), 6.95-7.05 (m, 1H), 7.10-7.20 (m, 1H), 7.35-7.40 (m, 2H), 7.60-7.75 (m, 2H), 8.10 (s, 1H)	638
II-25		2-Diethylamino-ethanesulfonic acid [3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl]-amide	3.7	see examples	(300 MHz, $CDCl_3$) δ 0.95-1.05 (m, 6H), 2.45-2.55 (m, 4H), 2.95-3.10 (m, 2H), 3.15-3.25 (m, 2H), 5.11 (s, 2H), 5.67 (s, 2H), 6.90-7.15 (m, 2H), 7.20-7.40 (m, 2H), 7.65-7.70 (m, 2H), 8.10 (s, 1H)	627
II-26		2-Morpholin-4-yl-ethanesulfonic acid [3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl]-amide	3.9	see examples	(300 MHz, $CDCl_3$) δ 2.30-2.50 (m, 2H), 2.90-3.00 (m, 2H), 3.20-3.40 (m, 2H), 3.50-3.75 (m, 4H), 5.21 (s, 2H), 5.67 (s, 2H), 6.95-7.05 (m, 1H), 7.10-7.20 (m, 1H), 7.30-7.50 (m, 2H), 7.67 (s, 1H), 7.74 (d, J = 7.5 Hz, 1 H), 8.12 (s, 1H)	641
II-27		2-Pyrrolidin-1-yl-ethanesulfonic acid [3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl]-amide	1.8	see examples	(300 MHz, $CDCl_3$) δ 1.62-1.82 (m, 4H), 2.40-2.55 (m, 4H), 2.82-3.00 (m, 2H), 3.25-3.35 (m, 2H), 5.24 (s, 2H), 5.67 (s, 2H), 6.95-7.05 (m, 1H), 7.10-7.20 (m, 1H), 7.25-7.40 (m, 2H), 7.63 (s, 1H), 7.73 (d, J = 7.1 Hz, 1 H), 8.12 (s, 1H)	625
II-28		2-Dimethylamino-ethanesulfonic acid [3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl]-amide	2.28	see examples	(300 MHz, $CDCl_3$) δ 2.27 (s, 6H), 2.88 (t, J = 6.4 Hz, 2H), 3.23 (t, J = 6.4 Hz, 2H), 5.08 (s, 2H), 5.67 (s, 2H), 7.00-7.45 (m, 4H), 7.66-7.75 (m, 2H), 8.11 (s, 1H)	499
II-29		2-[4-(2-Hydroxy-acetyl)-piperazin-1-yl]-ethanesulfonic acid [3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl]-amide	1.82	see examples	(300 MHz, $CDCl_3$) δ 2.43 (t, 4H), 2.82 (t, 2H), 3.20 (t, 2H), 3.33 (t, 2H), 3.54 (br s, 1H), 3.81 (t, 2H), 4.08 (s, 2H), 5.18 (br s, 2H), 5.67 (s, 2H), 7.00-7.45 (m, 4H), 7.65-7.75 (m, 2H), 8.11 (s, 1H)	697

No.	Structure	Name	Met IC_{50} (nM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-30		2-(Cyclopropylmethyl-amino)-ethanesulfonic acid [3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl]-amide	1.84	see examples	(300 MHz, $CDCl_3$) δ 0.07 (m, 2H), 0.44 (m, 2H), 0.89 (m, 1H), 2.45 (d, 2H), 3.16 (t, 2H), 3.29 (t, 2H), 5.27 (br s, 2H), 5.57 (s, 2H), 7.07 (m, 1H), 7.20 (m, 1H), 7.41 (m, 2H), 7.66 (s, 1H), 7.77 (m, 1H), 8.12 (s, 1H)	524
II-31		2-[(3R)-3-Hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid [3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl]-amide	2.18	see examples	(300 MHz, $CDCl_3$) δ 1.80 (m, 1H), 2.20 (m, 2H), 2.50 (m, 1H), 2.70-3.20 (m, 6H), 3.32 (m, 2H), 4.35 (m, 1H), 8.12 (s, 2H), 5.58 (s, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.40 (m, 2H), 7.73 (m, 2H), 8.15 (s, 1H)	540
II-32		2-Cyclopropylamino-ethanesulfonic acid [3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl]-amide	2.13	see examples	(300 MHz, $CDCl_3$) δ 0.25-0.50 (m, 4H), 2.09 (m, 1H), 3.15-3.40 (m, 4H), 5.37 (s, 2H), 5.68 (s, 2H), 7.07 (m, 1H), 7.18 (m, 1H), 7.42 (m, 2H), 7.82 (m, 1H), 7.77 (m, 1H), 8.13 (s, 1H)	510
II-33		4-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-benzoic acid		see examples		392
II-34		(4-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl)-[(2R')-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.18	see examples	(300 MHz, $CDCl_3$) δ 1.6-2.2 (m, 10 H), 2.65 (m, 4H), 3.50 (m, 2H), 4.42 (m, 1H), 4.86 (br s, 2H), 5.68 (d, J = 1.3 Hz, 2H), 7.05 (m, 1H), 7.19 (m, 1H), 7.67 (m, 2H), 7.99 (d, 2H), 8.12 (s, 1H)	528
II-35		4-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide	0.13	see examples	(300 MHz, $CDCl_3$) δ 1.87 (m, 4H), 2.73 (m, 4H), 2.85 (t, 2H), 3.64 (m, 2H), 4.91 (s, 2H), 5.69 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.89 (d, 2H), 7.99 (d, 2H), 8.13 (s, 1H)	499
II-36		(4-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl)-[(3S)-3-amino-pyrrolidin-1-yl]-methanone	0.37	see examples	(300 MHz, CD_3OD) δ 1.80-2.40 (m, 2H), 2.24 (s, 3H), 3.30-3.90 (m, 6H), 5.71 (s, 2H), 7.25 (m, 1H), 7.35 (m, 1H), 7.80 (m, 2H), 8.03 (d, 2H), 8.10 (s, 1H)	481
II-37		N-[2-(4-Acetyl-piperazin-1-yl)-ethyl]-4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-benzamide	1.35	see examples	(300 MHz, $CDCl_3$) δ 2.10 (s, 3H), 2.52 (m, 4H), 2.66 (t, 2H), 3.40-3.80 (m, 8H), 4.94 (s, 2H), 5.68 (s, 2H), 6.79 (brs, 1H), 7.05 (m, 1H), 7.20 (m, 1H), 7.84 (d, 2H), 8.00 (d, 2H), 8.14 (s, 1H)	545
II-38		4-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide	0.68	see examples	(300 MHz, $CDCl_3$) δ 1.91 (m, 6H), 2.72 (m, 4H), 2.82 (t, 2H), 3.61 (m, 2H), 4.93 (s, 2H), 5.69 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.89 (d, 2H), 7.97 (d, 2H), 8.12 (s, 1H), 8.73 (s, 1H)	503

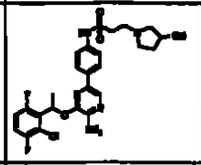
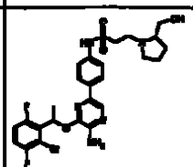
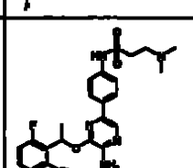
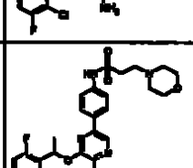
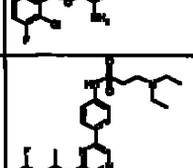
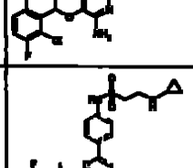
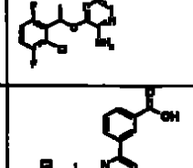
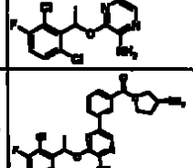
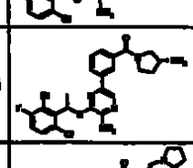
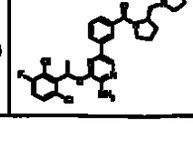
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-39		{4-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(3S)-3-dimethylamino-pyrrolidin-1-yl]-methanone	0.67	see examples	(300 MHz, $CDCl_3$) δ 1.70-2.10 (m, 1H), 2.24 (s, 3H), 2.34 (s, 3H), 2.80-2.90 (m, 1H), 3.30-4.00 (m, 4H), 4.90 (s, 2H), 5.68 (d, 2H), 7.10 (m, 1H), 7.20 (m, 1H), 7.60 (m, 2H), 7.97 (d, 2H), 8.13 (s, 1H)	469
II-40		{4-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(3R')-3-dimethylamino-pyrrolidin-1-yl]-methanone	0.48	see examples	(300 MHz, CD_3OD) δ 1.80-2.40 (m, 2H), 2.24 (s, 3H), 3.30-3.80 (m, 5H), 5.71 (s, 2H), 7.25 (m, 1H), 7.35 (m, 1H), 7.60 (m, 2H), 8.03 (d, 2H), 8.10 (s, 1H)	481
II-41		{4-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone	0.48	see examples	(300 MHz, $CDCl_3$) δ 0.9-1.2 (m, 6H), 2.2-3.2 (m, 8H), 4.91 (s, 2H), 5.69 (s, 2H), 7.10 (m, 1H), 7.20 (m, 1H), 7.48 (d, 2H), 7.97 (d, 2H), 8.12 (s, 1H)	469
II-42		{4-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.33	see examples	(300 MHz, $CDCl_3$) δ 1.60-3.10 (m, 17H), 4.89 (s, 2H), 5.68 (d, 2H), 7.10 (m, 1H), 7.20 (m, 1H), 7.47 (d, 2H), 7.96 (d, 2H), 8.11 (s, 1H)	523
II-43		4-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide	0.59	see examples	(300 MHz, $CDCl_3$) δ 1.83 (m, 2H), 2.60 (m, 6H), 3.61 (m, 2H), 3.76 (m, 4H), 4.93 (s, 2H), 5.70 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.86 (d, 2H), 8.00 (d, 2H), 8.14 (s, 1H)	518
II-44		4-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide	0.5	see examples	(300 MHz, $CDCl_3$) δ 1.80 (m, 2H), 2.07 (m, 2H), 2.22 (m, 2H), 2.34 (s, 3H), 2.88 (m, 2H), 4.04 (m, 2H), 4.92 (s, 2H), 5.69 (d, 2H), 6.03 (d, 1H), 7.05 (m, 1H), 7.20 (m, 1H), 7.82 (d, 2H), 7.98 (d, 2H), 8.13 (s, 1H)	489
II-45		4-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide	1.11	see examples	(300 MHz, CD_3OD) δ 2.68 (m, 6H), 3.60 (m, 2H), 3.75 (m, 4H), 5.72 (s, 2H), 7.25 (m, 1H), 7.35 (m, 1H), 7.88 (d, 2H), 8.06 (d, 2H), 8.12 (s, 1H)	504
II-46		{4-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone	0.66	see examples	(300 MHz, $CDCl_3$) δ 2.39 (s, 3H), 2.48 (m, 4H), 3.69(m, 4H), 4.89 (s, 2H), 5.69(s, 2H), 7.08 (m, 1H), 7.20 (m, 1H), 7.52 (d, 2H), 7.95(d, 2H), 8.09 (s, 1H)	474
II-47		3-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-benzoic acid		see examples		392

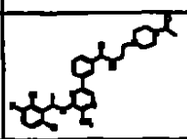
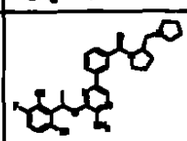
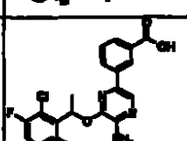
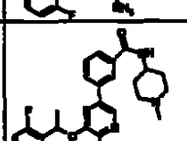
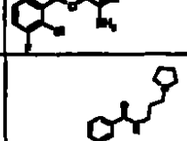
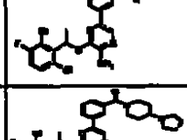
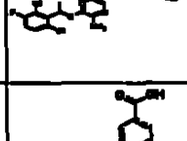
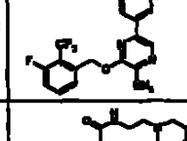
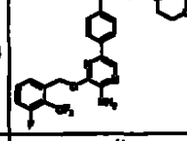
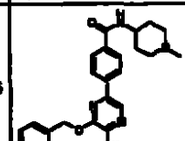
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-45		(3-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone	2.85	see examples	(300 MHz, $CDCl_3$) δ 2.39 (s, 3H), 2.46 (m, 4H), 3.66(m, 4H), 4.86 (br s, 2H), 5.57(s, 2H), 7.06 (m, 1H), 7.20 (m, 1H), 7.35 (d, 1H), 7.47 (t, 1H), 7.95(m, 2H), 8.10 (s, 1H)	474
II-46		(3-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl)-[(3*R*)-3-amino-pyrrolidin-1-yl]-methanone	1.02	see examples	(300 MHz, CD_3OD) δ 2.12 (m, 1H), 2.44 (m, 1H), 3.62-4.05 (m, 6H), 5.77(s, 2H), 7.24 (m, 1H), 7.35 (m, 1H), 7.54 (m, 2H), 8.02 (s, 1H), 8.12 (m, 2H)	460
II-50		(3-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl)-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone	0.91	see examples	(300 MHz, CD_3OD) δ 2.12 (m, 1H), 2.44 (m, 1H), 3.62-4.05 (m, 6H), 5.77(s, 2H), 7.24 (m, 1H), 7.35 (m, 1H), 7.54 (m, 2H), 8.02 (s, 1H), 8.12 (m, 2H)	460
II-51		(3-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl)-(3,5-dimethyl-piperazin-1-yl)-methanone	2.56	see examples	(300 MHz, $CDCl_3$) δ 0.99 (br d, 3H), 1.16 (br d, 3H), 2.42 (m, 1H), 2.70 (m, 1H), 2.84 (m, 1H), 2.93 (m, 1H), 3.66(m, 1H), 4.67 (m, 1H), 4.82 (br s, 2H), 5.59(s, 2H), 7.06 (m, 1H), 7.20 (m, 1H), 7.35 (m, 1H), 7.47 (t, 1H), 7.97(m, 2H), 8.10 (s, 1H)	488
II-52		3-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide	4.2	see examples	(300 MHz, $CDCl_3$) δ 1.82 (m, 2H), 2.50 (m, 4H), 2.58 (m, 2H), 3.67(m, 6H), 4.86 (br s, 2H), 5.58 (s, 2H), 7.05 (m, 1H), 7.19 (m, 1H), 7.48 (t, 1H), 7.70 (d, 1H), 7.90 (m, 1H), 8.05(d, 1H), 8.14 (s, 1H), 8.36 (t, *J* = 1.8 Hz, 1H)	519
II-53		(3-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.63	see examples	(300 MHz, $CDCl_3$) δ 1.60 (m, 2H), 1.90 (m, 4H), 1.66 (m, 2H), 2.00 (m, 2H), 2.32 (m, 1H), 2.61 (m, 4H), 2.66 (m, 2H), 3.00 (m, 2H), 3.82(m, 1H), 4.66 (m, 1H), 4.93 (br s, 2H), 5.56 (s, 2H), 7.06 (m, 1H), 7.18 (m, 1H), 7.32 (dt, 1H), 7.46 (t, 1H), 7.70 (d, 1H), 7.87 (m, 2H), 8.09(d, *J* = 3.6 Hz, 1H)	529
II-54		(3-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl)-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone	1.46	see examples	(300 MHz, $CDCl_3$) δ 1.66 (m, 1H), 2.10 (m, 1H), 2.21 (s, 3H), 2.31 (s, 3H), 2.76 (m, 1H), 3.42 (m, 1H), 3.64 (m, 2H), 3.92 (m, 1H), 4.83 (br s, 2H), 5.57 (s, 2H), 7.06 (m, 1H), 7.19 (m, 1H), 7.48 (m, 2H), 7.97 (m, 1H), 8.09(m, 2H)	488
II-55		3-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(2-pyrrolidin-1-yl-ethyl)-benzamide	1.9	see examples	(300 MHz, $CDCl_3$) δ 1.82 (m, 4H), 2.69 (m, 4H), 2.84 (m, 2H), 3.65 (m, 2H), 4.33 (br s, 2H), 5.58 (s, 2H), 7.06 (m, 1H), 7.19 (m, 1H), 7.22 (m, 1H), 7.49 (t, *J* = 7.7 Hz, 1H), 7.77 (d, *J* = 7.8 Hz, 1H), 8.04 (dt, *J* = 7.9 Hz, 1.5 Hz, 1H), 8.13 (s, 1H), 8.39(t, *J* = 1.5 Hz, 1H)	488
II-56		3-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide	0.9	see examples	(300 MHz, $CDCl_3$) δ 1.71 (m, 2H), 2.11(m, 2H), 2.28 (t, 2H), 2.95 (m, 2H), 4.11 (m, 1H), 4.89 (s, 2H), 5.59(s, 2H), 6.26 (m, 1H), 7.06 (m, 1H), 7.18 (m, 1H), 7.48(t, 1H), 7.88 (d, 1H), 8.06 (d, 1H), 8.11 (s, 1H), 8.35 (s, 1H)	488
II-57		(3-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl)-[(2*S*)-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.63	see examples	(300 MHz, $CDCl_3$) δ 2.02 (m, 10H), 2.76(m, 4H), 3.49 (m, 2H), 4.81 (m, 1H), 4.86 (s, 2H), 5.59(s, 2H), 7.06 (m, 1H), 7.20 (m, 1H), 7.48 (m, 2H), 7.98(m, 1H), 8.07 (m, 1H), 8.11 (s, 1H)	528
II-58		3-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide	2.5	see examples	(300 MHz, CD_3OD) δ 2.61 (m, 4H), 2.68 (t, 2H), 3.56 (t, 2H), 3.69 (m, 4H), 5.72 (s, 2H), 7.20 (m, 1H), 7.35 (m, 1H), 7.52 (t, 1H), 7.76 (d, 1H), 8.12 (m, 2H), 8.41(s, 1H)	504
II-59		*N*-[2-(4-Acetyl-piperazin-1-yl)-ethyl]-3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-benzamide	2.77	see examples	(300 MHz, CD_3OD) δ 2.08 (s, 3H), 2.59 (m, 6H), 3.57 (m, 6H), 5.71 (s, 2H), 7.21 (m, 1H), 7.37 (m, 1H), 7.50 (t, 1H), 7.75 (d, 1H), 8.06 (m, 2H), 8.39(s, 1H)	545

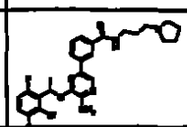
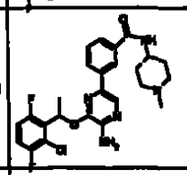
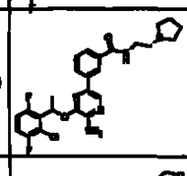
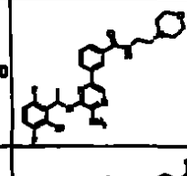
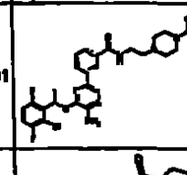
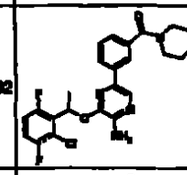
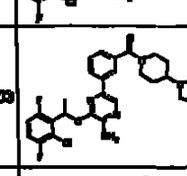
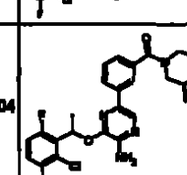
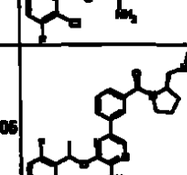
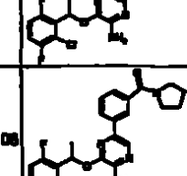
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-80		3-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(3-pyrrolidin-1-yl-propyl)-benzamide	1.48	see examples	(300 MHz, $CDCl_3$) δ 1.79 (m, 4H), 1.88 (t, 2H), 2.55 (m, 4H), 2.78 (t, 2H), 3.55 (m, 2H), 4.85 (s, 2H), 5.89(s, 2H), 7.06 (m, 1H), 7.21 (m, 1H), 7.45(t, 1H), 7.55 (d, 1H), 8.08 (d, 1H), 8.15 (s, 1H), 8.40 (s, 1H), 8.68 (m, 1H)	502
II-81		3-(2-Chloro-3,6-difluoro-benzyloxy)-5-(1*H*-indol-5-yl)-pyrazin-2-ylamine		see examples		387
II-82		3-(2-Chloro-3,6-difluoro-benzyloxy)-5-(3-pyrrolidin-1-ylmethyl-1*H*-indol-5-yl)-pyrazin-2-ylamine	0.35	see examples	(300 MHz, $CDCl_3$) δ 1.78 (m, 4H), 2.58 (m, 4H), 3.89 (s, 2H), 4.89 (s, 2H), 5.89(s, 2H), 7.08 (m, 1H), 7.16 (m, 2H), 7.38 (d, 1H), 7.79(d, 1H), 8.08 (s, 1H), 8.18 (s, 1H), 8.79(s, 1H)	470
II-83		3-(2-Chloro-3,6-difluoro-benzyloxy)-5-(3-diethylaminomethyl-1*H*-indol-5-yl)-pyrazin-2-ylamine	0.73	see examples	(300 MHz, $CDCl_3$) δ 1.11 (m, 6H), 2.69 (m, 4H), 3.90 (s, 2H), 4.89(s, 2H), 5.77 (s, 2H), 7.02 (m, 1H), 7.21 (m, 2H), 7.45 (d, 1H), 7.89(d, 1H), 8.22 (m, 3H)	472
II-84		1-(4-{5-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-1*H*-indol-3-ylmethyl}-piperazin-1-yl)-ethanone	1.5	see examples	(300 MHz, $CDCl_3$) δ 2.06 (s, 3H), 2.55 (m, 4H), 3.45 (m, 2H), 3.84(m, 2H), 3.91 (s, 2H), 4.78 (s, 2H), 5.71(s, 2H), 7.06 (m, 1H), 7.16 (m, 2H), 7.31 (d, 1H), 7.79(d, 1H), 8.04 (s, 1H), 8.22 (s, 1H), 8.49(s, 1H)	527
II-85		3-(2-Chloro-3,6-difluoro-benzyloxy)-5-[3-(2,6-dimethyl-morpholin-4-ylmethyl)-1*H*-indol-5-yl]-pyrazin-2-ylamine	2.4	see examples	(300 MHz, $CDCl_3$) δ 1.11 (d, 6H), 1.98 (m, 2H), 2.69 (m, 2H), 3.07(m, 4H), 4.75 (s, 2H), 5.78 (s, 2H), 7.09 (m, 1H), 7.27 (m, 2H), 7.49 (d, 1H), 7.89(d, 1H), 8.19 (s, 1H), 8.25 (s, 2H)	514
II-86		*N*-(1-{5-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-1*H*-indol-3-ylmethyl}-(3*S*)-pyrrolidin-3-yl)-acetamide	0.55	see examples	(300 MHz, $CDCl_3$) δ 1.69 (m, 1H), 1.88(s, 3H), 2.39 (m, 2H), 2.75 (m, 2H), 3.08(m, 1H), 3.85 (m, 2H), 4.50 (m, 1H), 4.79 (s, 2H), 5.78 (s, 2H), 6.01 (m, 1H), 7.05 (m, 1H), 7.18 (m, 2H), 7.42 (d, 1H), 7.79(d, 1H), 8.12 (s, 1H), 8.21 (s, 1H), 8.28 (s, 1H)	527
II-87		3-(2-Chloro-3,6-difluoro-benzyloxy)-5-(3-piperidin-1-ylmethyl-1*H*-indol-5-yl)-pyrazin-2-ylamine	0.81	see examples	(300 MHz, $CDCl_3$) δ 1.49 (m, 2H), 1.71 (m, 4H), 2.55(m, 4H), 3.69 (s, 2H), 4.79 (s, 2H), 5.89(s, 2H), 7.05 (m, 1H), 7.18 (m, 1H), 7.31 (s, 1H), 7.42 (d, 1H), 7.79(d, 1H), 8.08 (s, 1H), 8.18(s, 1H), 8.69 (br s, 1H)	484
II-88		3-(2-Chloro-3,6-difluoro-benzyloxy)-5-(3-morpholin-4-ylmethyl-1*H*-indol-5-yl)-pyrazin-2-ylamine	1.15	see examples	(300 MHz, $CDCl_3$) δ 2.72 (m, 4H), 3.80 (m, 6H), 4.73 (s, 2H), 5.73 (s, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.48 (d, 1H), 7.80 (dd, 1H), 8.12 (s, 1H), 8.25 (s, 1H)	486

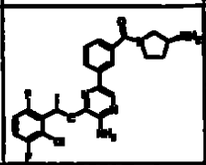
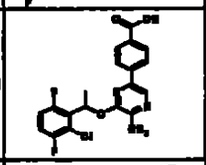
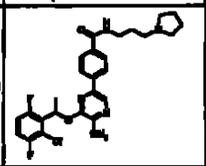
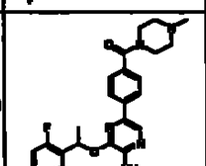
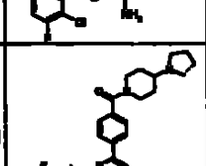
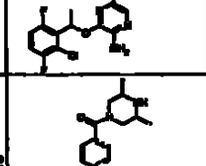
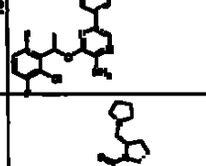
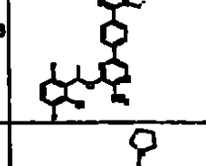
No.	Structure	Name	Mast IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-69		3-[1-(2-Chloro-3,6-difluoro-phenyl)-2-methyl-propoxy]-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyrazin-2-ylamine	10.58	see examples	(400 MHz, DMSO-d_6) δ 0.88 (d, 3H), 1.19 (d, 3H), 2.47 (m, 4H), 2.88 (m, 1H), 2.88 (t, 2H), 3.58 (t, 4H), 4.07 (t, 2H), 5.96 (d, 1H), 6.28 (s, 2H), 6.89 (d, 2H), 7.28 (m, 1H), 7.39 (m, 1H), 7.63 (d, 2H), 7.95 (s, 1H)	519
II-70	 TFA	3-[1-(2-Chloro-3,6-difluoro-phenyl)-ethoxy]-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyrazin-2-ylamine; compound with trifluoro-acetic acid	0.51	see examples	(400 MHz, DMSO-d_6) δ 1.76 (d, 3H), 3.21 (m, 2H), 3.51 (m, 2H), 3.54 (m, 2H), 3.74 (m, 2H), 3.98 (m, 2H), 4.36 (t, 2H), 6.34 (br s, 2H), 6.42 (m, 1H), 6.97 (d, 2H), 7.25 (m, 1H), 7.38 (m, 1H), 7.86 (d, 2H), 7.86 (s, 1H)	491
II-71	 TFA	3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyrazin-2-ylamine; compound with trifluoro-acetic acid	0.3	see examples	(400 MHz, DMSO-d_6) δ 1.79 (d, 3H), 3.21 (m, 2H), 3.48 (m, 2H), 3.57 (m, 2H), 3.74 (m, 2H), 3.98 (m, 2H), 4.36 (t, 2H), 6.34 (br s, 2H), 6.49 (m, 1H), 6.94 (d, 2H), 7.37 (t, 1H), 7.48 (m, 1H), 7.86 (d, 2H), 7.96 (s, 1H)	491
II-72		*N*-(4-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-methanesulfonamide		see examples	(400 MHz, DMSO-d_6) δ 1.78 (d, 3H), 2.96 (s, 3H), 6.41 (m, 3H), 7.18 (d, 2H), 7.39 (m, 1H), 7.37 (m, 1H), 7.84 (d, 2H), 8.00 (s, 1H), 8.72 (s, 1H)	455
II-73		2-Pyrrolidin-1-yl-ethanesulfonic acid (4-[5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-amide		see examples	(300 MHz, $CDCl_3$) δ 1.0- (m, 7H), 2.56 (m, 4H), 3.04 (m, 2H), 3.25 (m, 2H), 4.84 (br s, 2H), 6.71 (q, 1H), 6.95 (m, 2H), 7.21 (d, 2H), 7.72 (d, 2H), 7.96 (s, 1H)	538
II-74		2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid (4-[5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-amide		see examples	(300 MHz, $CDCl_3$) δ 1.60 (m, 2H), 1.82 (m, 5H), 2.23 (m, 2H), 2.77 (m, 2H), 2.89 (t, 2H), 3.29 (t, 2H), 3.74 (m, 1H), 5.07 (br s, 2H), 6.70 (q, 1H),7.00 (m, 2H), 7.24 (d, 2H), 7.73 (d, 2H), 7.94 (s, 1H)	568
II-75		2-Piperidin-1-yl-ethanesulfonic acid (4-[5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-amide		see examples	(300 MHz, $CDCl_3$) δ 1.49 (m, 2H), 1.61 (m, 4H), 1.83 (d, 3H), 2.60 (m, 4H), 2.96 (m, 2H), 3.20 (m, 2H), 4.95 (br s, 2H), 6.70 (q, 1H), 7.00 (m, 2H), 7.24 (d, 2H), 7.74 (d, 2H), 7.96 (s, 1H)	552
II-76		2-(Cyclopropylmethyl-amino)-ethanesulfonic acid (4-[5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-amide		see examples	(300 MHz, $CDCl_3$) δ 0.14 (m, 2H), 0.50 (m, 2H), 0.85 (m, 1H), 1.82 (d, 3H), 2.49 (m, 2H), 3.30 (m, 4H), 4.73 (br s, 1H), 5.02 (br s, 2H), 6.71 (q, 1H), 7.00 (m, 2H), 7.25 (d, 2H), 7.74 (d, 2H), 7.96 (s, 1H)	538

123

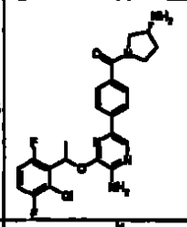
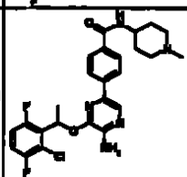
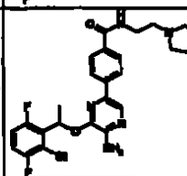
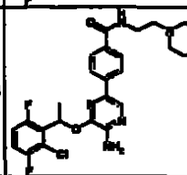
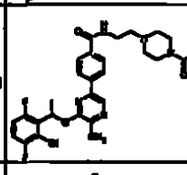
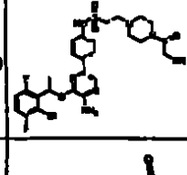
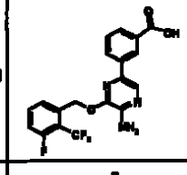
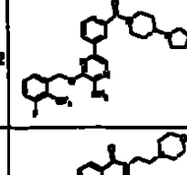
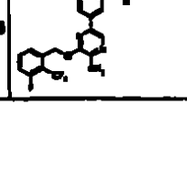
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-77		2-[(3R)-3-Hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide		see examples	(300 MHz, $CDCl_3$) δ 1.79 (m, 1H), 1.82 (d, 3H), 2.28 (m, 2H), 2.64 (m, 1H), 2.82 (m, 1H), 2.96 (m, 2H), 3.09 (m, 1H), 3.26 (m, 2H), 4.44 (m, 1H), 4.94 (br s, 1H), 6.70 (q, 1H), 7.00 (m, 2H), 7.29 (d, 2H), 7.73 (d, 2H), 7.96 (s, 1H)	554
II-78		2-[(2S)-2-Hydroxymethyl-pyrrolidin-1-yl]-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide		see examples	(300 MHz, $CDCl_3$) δ 1.79 (m, 4H), 1.82 (d, 3H), 2.15 (m, 1H), 2.68 (m, 2H), 2.93 (m, 2H), 3.35 (m, 1H), 3.48 (m, 1H), 3.84 (m, 1H), 3.92 (m, 1H), 4.97 (br s, 1H), 6.70 (q, 1H), 7.00 (m, 2H), 7.28 (d, 2H), 7.71 (d, 2H), 7.96 (s, 1H)	568
II-79		2-Dimethylamino-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide		see examples	(300 MHz, $CDCl_3$) δ 1.82 (d, 3H), 2.29 (s, 6H), 2.65 (t, 2H), 3.21 (t, 2H), 5.00 (br s, 2H), 6.71 (q, 1H), 7.00 (m, 2H), 7.23 (d, 2H), 7.74 (d, 2H), 7.96 (s, 1H)	512
II-80		2-Morpholin-4-yl-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide		see examples	(300 MHz, $CDCl_3$) δ 1.82 (d, 3H), 2.48 (m, 4H), 2.90 (m, 2H), 3.27 (m, 2H), 3.71 (m, 4H), 4.92 (br s, 2H), 6.71 (q, 1H), 7.00 (m, 2H), 7.24 (d, 2H), 7.74 (d, 2H), 7.97 (s, 1H)	554
II-81		2-Diethylamino-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide		see examples	(300 MHz, $CDCl_3$) δ 1.07 (t, 6H), 1.82 (d, 3H), 2.60 (q, 4H), 3.02 (t, 2H), 3.22 (t, 2H), 4.85 (br s, 2H), 6.71 (q, 1H), 7.00 (m, 2H), 7.22 (d, 2H), 7.74 (d, 2H), 7.96 (s, 1H)	540
II-82		2-Cyclopropylamino-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide		see examples	(300 MHz, $CDCl_3$) δ 0.35 (m, 2H), 0.50 (m, 2H), 1.82 (d, 3H), 2.15 (m, 1H), 3.24 (m, 4H), 4.95 (br s, 2H), 6.71 (q, 1H), 7.00 (m, 2H), 7.21 (d, 2H), 7.74 (d, 2H), 7.97 (s, 1H)	510
II-83		3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-benzoic acid	1.36	see examples		423
II-84		(3-{5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-[(3S)-3-amino-pyrrolidin-1-yl]-m-ethanone	0.089	see examples	(300MHz, MeOD) δ 7.84 (d, 1H), 7.71 (m, 2H), 7.38 (m, 3H), 7.10 (m, 1H), 6.80 (m, 1H), 4.86 (s, 2H), 4.20 (m, 1H), 3.45-3.89 (m, 4H), 1.82 (d, 3H), 1.34 (m, 1H), 0.89 (m, 1H)	492
II-85		(3-{5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-[(3R)-3-amino-pyrrolidin-1-yl]-m-ethanone	0.11	see examples	(300MHz, MeOD) δ 7.84 (d, 1H), 7.71 (m, 2H), 7.38 (m, 3H), 7.10 (m, 1H), 6.80 (m, 1H), 4.86 (s, 2H), 4.20 (t, 1H), 3.45-3.89 (m, 4H), 1.82 (d, 3H), 1.34 (m, 1H), 0.89 (m, 1H)	492
II-86		(3-{5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-[(2R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.15	see examples	(300MHz, $CDCl_3$) δ 8.04 (d, 1H), 7.84 (d, 2H), 7.30 (d, 2H), 7.15 (dd, 1H), 6.99 (t, 1H), 5.89 (m, 1H), 4.89 (s, 2H), 4.44 (s, 1H), 3.89 (m, 1H), 3.65 (m, 1H), 3.30 (m, 2H), 2.85 (m, 3H), 1.82 (d, 3H), 0.89-2.20 (m, 9H)	558

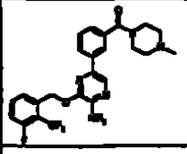
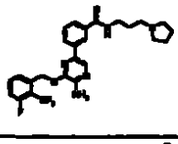
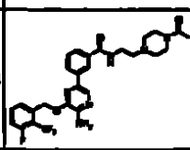
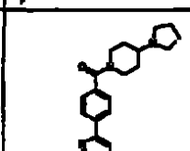
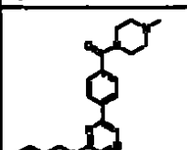
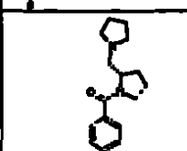
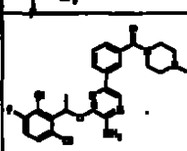
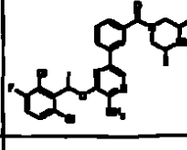
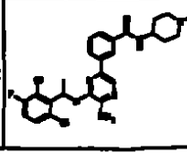
No.	Structure	Name	Mat IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-87		N-[2-(4-Acetyl-piperazin-1-yl)-ethyl]-3-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-benzamide	0.189	see examples	(300MHz, $CDCl_3$) δ 8.04 (d, 1H), 7.89 (s, 1H), 7.78 (d, 1H), 7.60 (d, 1H), 7.34 (m, 2H), 7.18 (t, 1H), 6.72 (bm, 1H), 4.89 (s, 2H), 4.86 (m, 6H), 3.21 (d, 2H), 2.80 (t, 1H), 2.65 (dd, 1H), 2.09 (s, 3H), 1.80 (d, 4H)	575
II-88		(3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-[(2S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone	0.17	see examples	(300MHz, MeOD) δ 8.04 (d, 1H), 7.84 (d, 2H), 7.35 (m, 3H), 7.20 (m, 1H), 6.80 (m, 1H), 4.89 (s, 2H), 4.44 (s, 1H), 3.59 (m, 1H), 3.30 (m, 1H), 3.25 (s, 2H), 3.16 (m, 3H), 1.82 (d, 3H), 0.86-2.82 (m, 9H)	559
II-89		3-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-benzoic acid		see examples		406
II-90		3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(1-methyl-piperidin-4-yl)-benzamide	0.21	see examples	(300 MHz, $CDCl_3$) δ 8.20 (s, 1H), 8.08 (s, 1H), 7.89 (d, 1H), 7.75 (d, 1H), 7.44 (t, 1H), 7.01 (m, 2H), 6.78 (m, 1H), 6.20 (s, 1H), 4.98 (s, 2H), 4.09 (m, 1H), 2.97 (m, 2H), 2.39 (s, 3H), 2.29 (t, 2H), 2.12 (m, 2H), 1.90 (d, 3H), 1.78 (m, 2H)	502
II-91		3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide	0.16	see examples	(300 MHz, CD_3OD) δ 8.15 (s, 1H), 7.98 (s, 1H), 7.80 (d, 1H), 7.61 (d, 1H), 7.35 (m, 2H), 7.09 (t, 1H), 6.89 (m, 1H), 3.44 (t, 2H), 2.65 (m, 6H), 1.88 (d, 3H), 1.80 (m, 6H)	532
II-92		(3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.15	see examples	(300 MHz, CD_3OD) δ 7.99 (s, 1H), 7.76 (d, 1H), 7.55 (m, 1H), 7.41 (m, 2H), 7.21 (d, 1H), 7.12 (t, 1H), 6.81 (m, 1H), 4.56 (m, 2H), 3.62 (m, 1H), 3.08 (m, 2H), 2.89 (m, 6H), 2.45 (m, 2H), 2.12 (m, 2H), 1.99 (d, 3H), 1.48(m, 2H)	558
II-93		4-[5-Amino-6-[3-fluoro-2-(trifluoromethyl-benzyloxy)-pyrazin-2-yl]-benzoic acid		see examples		458
II-94		4-[5-Amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide	0.22	see examples	(300MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.92 (d, 2H), 7.84 (d, 2H), 7.50 (m, 1H), 7.42 (m, 1H), 7.20 (m, 1H), 6.75 (s, 1H), 6.70 (s, 2H), 4.97 (s, 2H), 3.74 (m, 4H), 3.56 (m, 2H), 2.62 (m, 2H), 2.62 (s, 4H)	520
II-95		4-[5-Amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-N-(1-methyl-piperidin-4-yl)-benzamide	0.091	see examples	(300MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.92 (d, 2H), 7.84 (d, 2H), 7.50 (m, 1H), 7.42 (m, 1H), 7.20 (m, 1H), 6.04 (d, 1H), 5.75 (s, 2H), 5.01 (s, 2H), 4.0 (m, 1H), 2.88 (d, 2H), 2.30 (s,3H), 2.20 (t, 2H), 2.12 (d, 2H), 1.89 (m, 2H)	504
II-96		3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide	0.15	4 se in Example II-84	(300MHZ, CD3OD) δ 8.18 (s, 1H), 7.98 (s, 1H), 7.80 (d, 1H), 7.61 (d, 1H), 7.35 (m, 2H), 7.12 (t, 1H), 6.75 (s, 1H), 3.44 (t, 2H), 2.65 (m, 6H), 1.88 (d, 3H), 1.80 (m, 6H).	532

No.	Structure	Name	Met IC_{50} (uM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-97		3-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide	0.35	4 as in Example II-90	(300MHZ, CDCl3) δ 8.36 (s, 1H), 8.18 (s, 2H), 7.82 (m, 2H), 7.48 (t, 1H), 7.02 (m, 2H), 6.78 (q, 1H), 4.66 (s, 2H), 3.72 (m, 2H), 3.16 (m, 2H), 2.83 (m, 2H), 2.22 (m, 2H), 2.08 (m, 4H), 1.83 (d, 3H), 1.70 (m, 2H).	516
II-98		3-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(1-methyl-piperidin-4-yl)-benzamide	0.21	4 as in Example II-90	(300MHZ, CDCl3) δ 8.20 (s, 1H), 8.06 (s, 1H), 7.88 (d, 1H), 7.76 (d, 1H), 7.44 (t, 1H), 7.01 (m, 2H), 6.78 (q, 1H), 6.20 (bd, 1H), 4.66 (s, 2H), 4.09 (m, 1H), 2.97 (m, 2H), 2.39 (s, 3H), 2.29 (m, 2H), 2.12 (m, 2H), 1.90 (d, 3H), 1.78 (m, 2H).	502
II-99		3-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide	0.18	4 as in Example II-90	(300MHZ, CDCl3) δ 8.18 (s, 1H), 8.09 (s, 1H), 7.88 (d, 1H), 7.76 (d, 1H), 7.48 (t, 1H), 7.06 (bm, 1H), 6.98 (m, 2H), 6.75 (q, 1H), 5.06 (s, 2H), 3.66 (m, 2H), 2.88 (m, 2H), 2.66 (m, 4H), 1.88 (m, 7H).	502
II-100		3-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide	0.31	4 as in Example II-90	(300MHZ, CDCl3) δ 8.17 (s, 1H), 8.08 (s, 1H), 7.88 (d, 1H), 7.86 (d, 1H), 7.48 (t, 1H), 6.98 (m, 2H), 6.80 (bt, 1H), 6.74 (q, 1H), 5.02 (s, 2H), 3.78 (m, 4H), 3.68 (m, 2H), 2.68 (m, 2H), 2.58 (m, 4H), 1.86 (d, 3H).	518
II-101		N-[2-(4-Acetyl-piperazin-1-yl)-ethyl]-3-[5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-benzamide	0.64	4 as in Example II-90	(300MHZ, CDCl3) δ 8.16 (s, 1H), 8.03 (s, 1H), 7.86 (d, 1H), 7.83 (d, 1H), 7.40 (t, 1H), 6.98 (m, 3H), 6.71 (q, 1H), 5.13 (s, 2H), 3.69 (m, 4H), 3.61 (m, 2H), 2.60 (m, 2H), 2.66 (m, 4H), 2.08 (s, 3H), 1.83 (d, 3H).	559
II-102		(3-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone		4 as in Example II-90	(300MHZ, CDCl3) δ 8.02 (s, 1H), 7.82 (m, 2H), 7.41 (t, 1H), 7.28 (m, 1H), 6.96 (m, 2H), 6.71(q, 1H), 5.00 (s, 2H), 3.85 (m, 2H), 3.48 (m, 2H), 2.36 (m, 4H), 2.33 (s, 3H), 1.83 (d, 3H).	488
II-103		(3-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-(1-pyrrolidin-1-yl-piperidin-1-yl)-methanone		4 as in Example II-90	(300MHZ, CDCl3) δ 8.02 (s, 1H), 7.80 (m, 2H), 7.41 (t, 1H), 7.29 (m, 1H), 6.96 (m, 2H), 6.69 (q, 1H), 4.97 (s, 2H), 4.72 (m, 1H), 3.83 (m, 1H), 2.81 (m, 7H), 1.83 (d, 3H), 2.10-1.70 (m, 8H).	542
II-104		(3-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone		4 as in Example II-90	(300MHZ, CDCl3) δ 8.03 (s, 1H), 7.80 (m, 2H), 7.41 (t, 1H), 7.29 (m, 1H), 6.96 (m, 2H), 6.70 (q, 1H), 5.00 (s, 2H), 4.66 (m, 1H), 3.86 (m, 1H), 2.75 (m, 3H), 2.42 (m, 1H), 1.83 (d, 3H), 1.57(m, 1H), 1.15 (m, 3H), 0.96 (m, 3H).	502
II-105		(3-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-((S)-3-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone		4 as in Example II-90	(300MHZ, CDCl3) δ 8.04 (s, 1H), 7.83 (m, 2H), 7.39 (m, 2H), 6.98 (m, 2H), 6.70 (q, 1H), 5.00 (s, 2H), 4.47 (m, 1H), 3.50 (m, 2H), 3.00 (m, 6H), 2.30 (m, 3H), 2.00 (m, 5H), 1.83 (d, 3H), 1.53 (m, 1H).	542
II-106		(3-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone		4 as in Example II-90	(300MHZ, CDCl3) δ 8.02 (s, 1H), 7.83 (m, 2H), 7.40 (m, 2H), 6.98 (m, 2H), 6.70 (q, 1H), 4.96 (s, 2H), 3.76 (m, 4H), 3.61-3.15 (m, 1H), 2.15 (m, 1H), 1.85 (d, 3H), 1.95-1.75 (m, 3H).	300

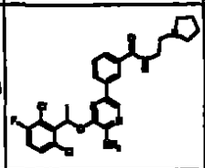
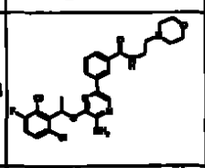
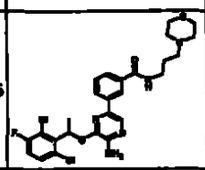
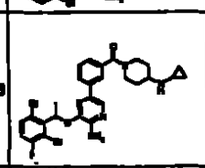
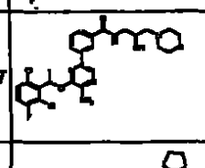
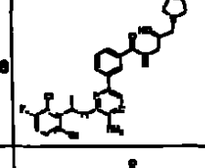
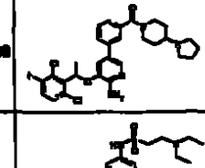
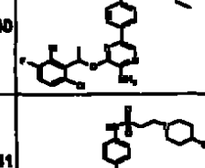
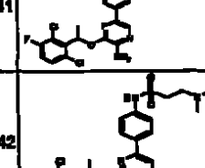
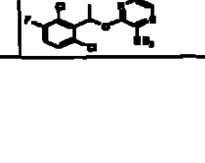
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-107		(3-{5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone		4 as in Example II-99	(300MHZ, CDCl3) δ 8.02 (s, 1H), 7.83 (m, 2H), 7.40 (m, 2H), 6.98 (m, 2H), 6.70 (q, 1H), 4.98 (s, 2H), 3.75 (m, 4H), 3.61-3.15 (m, 1H), 2.16 (m, 1H), 1.83 (d, 3H), 1.95-1.75 (m, 3H).	500
II-108		4-{5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-benzoic acid		3 as in Example I-211		406
II-109		4-{5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide	0.1	4 as in Example II-109	(300MHZ, CDCl3) δ 8.28 (bm, 1H), 8.04 (m, 3H), 7.84 (d, 2H), 6.95 (m, 2H), 6.71 (q, 1H), 5.03 (s, 2H), 3.85 (m, 2H), 3.72 (m, 2H), 3.18 (m, 2H), 2.82 (m, 2H), 2.25 (m, 4H), 2.08 (m, 2H), 1.87 (d, 3H).	616
II-110		(4-{5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone	0.16	4 as in Example II-109	(300MHZ, CDCl3) δ 7.99 (s, 1H), 7.78 (d, 2H), 7.43 (d, 2H), 7.29 (m, 1H), 6.85 (t, 1H), 6.94 (q, 1H), 5.07 (s, 2H), 3.76 (m, 2H), 3.50 (m, 2H), 2.43 (m, 4H), 2.33 (s, 3H), 1.84 (d, 3H).	488
II-111		(4-{5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.17	4 as in Example II-109	(300MHZ, CDCl3) δ 8.02 (s, 1H), 7.81 (d, 2H), 7.40 (d, 2H), 6.99 (m, 2H), 6.71 (q, 1H), 5.02 (s, 2H), 4.64 (m, 1H), 3.85 (m, 1H), 2.99 (m, 2H), 2.57 (m, 4H), 2.35 (m, 1H), 1.90 (m, 6H), 1.62 (m, 2H).	542
II-112		4-{5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl}-((3F,5S)-3,5-dimethyl-piperazin-1-yl)-methanone	0.19	4 as in Example II-109	(300MHZ, CDCl3) δ 8.02 (s, 1H), 7.81 (d, 2H), 7.38 (d, 2H), 6.99 (m, 2H), 6.71 (q, 1H), 4.99 (s, 2H), 4.66 (m, 1H), 3.85 (m, 1H), 2.88 (m, 2H), 2.68 (m, 1H), 2.41 (m, 1H), 1.84 (d, 3H), 1.84 (m, 1H), 1.16 (s, 3H), 1.06 (s, 3H).	502
II-113		(4-{5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.16	4 as in Example II-109	(300MHZ, CDCl3) δ 8.07 (s, 1H), 7.81 (d, 2H), 7.53 (d, 2H), 6.95 (m, 2H), 6.69 (q, 1H), 4.99 (s, 2H),4.45 (m, 1H), 3.55 (m, 2H), 2.95 (m, 4H), 1.90-2.3 (m, 9H),1.82 (d, 3H), 1.65 (m, 1H).	542
II-114		(4-{5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.13	4 as in Example II-109	(300MHZ, CDCl3) δ 8.02 (s, 1H), 7.81 (d, 2H), 7.53 (d, 2H), 6.95 (m, 2H), 6.69 (q, 1H), 4.99 (s, 2H),4.45 (m, 1H), 3.55 (m, 2H), 2.95 (m, 4H), 2.21 (m, 2H), 1.92 (m, 6H),1.82 (d, 3H), 1.59 (m, 1H).	542

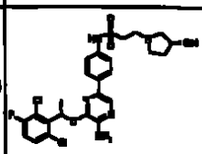
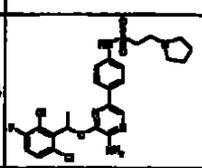
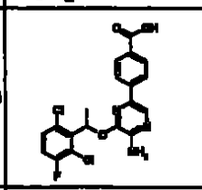
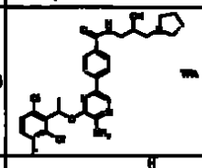
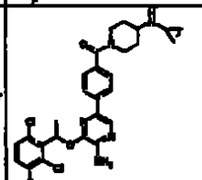
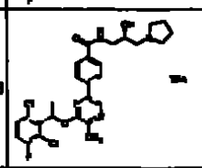
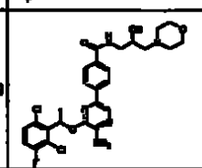
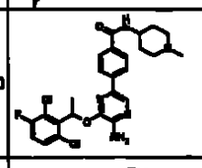
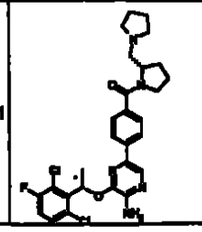
129

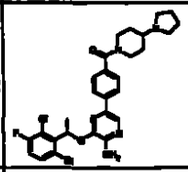
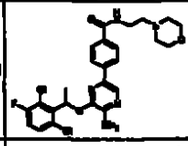
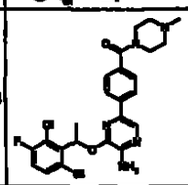
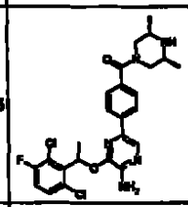
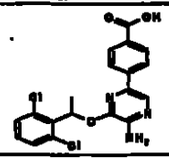
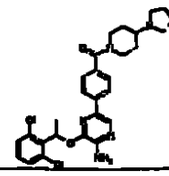
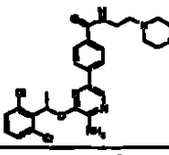
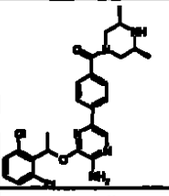
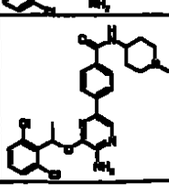
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-115		(4-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone	0.078	4 as in Example II-109	(300MHZ, CD3OD) δ 8.02 (s, 1H), 7.81 (d, 2H), 7.53 (d, 2H), 7.01 (m, 2H), 6.69 (q, 1H), 4.91 (s, 2H),3.85 (m, 1H), 3.71 (m, 2H), 3.55 (m, 1H), 2.18 (m, 1H), 1.85 (d, 3H), 1.75 (m, 1H), 1.42 (m, 3H).	574
II-116		4-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(1-methyl-piperidin-4-yl)-benzamide	0.19	4 as in Example II-109	(300MHZ, CDCl3) δ 8.06 (s, 1H), 7.82 (m, 4H), 7.00 (m, 2H), 6.72 (m, 2H), 5.04 (s, 2H), 4.09 (m, 1H), 2.97 (m, 2H), 2.39 (s, 3H), 2.29 (m, 2H), 2.12 (m, 2H), 1.90 (d, 3H), 1.79 (m, 2H).	602
II-117		4-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide	0.11	4 as in Example II-109	(300MHZ, CDCl3) δ 8.06 (s, 1H), 7.82 (m, 4H), 7.00 (m, 2H), 6.72 (m, 2H), 5.04 (s, 2H), 3.69 (m, 2H), 2.69 (m, 2H), 2.58 (m, 4H), 1.86 (m, 7H).	602
II-118		4-[5-Amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide	0.26	4 as in Example II-109	(300MHZ, CDCl3) δ 8.06 (s, 1H), 7.82 (m, 4H), 7.00 (m, 2H), 6.72 (m, 2H), 5.04 (s, 2H), 3.78 (m, 4H), 3.56 (m, 2H), 2.62 (t, 2H), 2.52 (m, 4H), 1.82 (d, 3H).	518
II-119		N-[2-(4-Acetyl-piperazin-1-yl)-ethyl]-4-[5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-benzamide	0.48	4 as in Example II-109	(300MHZ, CDCl3) δ 8.06 (s, 1H), 7.82 (m, 4H), 7.00 (m, 2H), 6.70 (m, 2H), 5.03 (s, 2H), 3.82 (m, 4H), 3.50 (m, 2H), 2.65 (t, 2H), 2.52 (m, 4H), 2.10 (s, 3H), 1.83 (d, 3H).	559
II-120		2-{1-(2-Hydroxy-acetyl)-piperazin-1-yl}-ethanesulfonic acid (4-[5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-amide	0.19	3 as in Example I-243	(300MHZ, CDCl3) δ 7.98 (s, 1H), 7.78 (d, 2H), 7.31 (m, 3H), 7.08 (m, 1H), 6.95 (m, 1H), 6.70 (q, 1H), 5.02 (s, 2H), 4.14 (s, 2H), 3.61 (m, 2H), 3.25 (m, 4H), 2.91 (m, 2H), 2.44 (m, 4H), 1.83 (d, 3H).	611
II-121		3-[5-Amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-benzoic acid		3 as in Example I-211		408
II-122		(3-[5-Amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.19	4 as in Example II-122	(300MHZ, CDCl3) δ 8.09 (s, 1H), 7.86 (m, 2H), 7.56 (m, 1H), 7.44 (t, 1H), 7.34 (d, 1H), 7.21 (t, 1H), 5.69 (s, 2H), 4.92 (s, 2H), 4.70 (m, 1H), 3.82 (m, 1H), 3.08 (m, 1H), 2.96 (m, 1H), 2.85 (m, 4H), 2.29 (m, 1H), 1.82 (m, 1H), 1.81 (m, 6H), 1.55 (m, 2H).	544
II-123		3-[5-Amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-N-(2-[ethyl-(2-methoxy-ethyl)-amino]-ethyl)-benzamide	0.46	4 as in Example II-122	(300MHZ, CDCl3) δ 8.34 (s, 1H), 8.14 (s, 1H), 8.01 (d, 1H), 7.88 (d, 1H), 7.53 (m, 1H), 7.50 (t, 1H), 7.46 (d, 1H), 7.21 (t, 1H), 6.79 (bm, 1H), 5.72 (s, 2H), 4.92 (s, 2H), 3.72 (m, 4H), 3.61 (m, 2H), 2.66 (m, 2H), 2.55 (m, 4H).	620

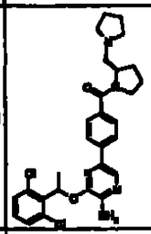
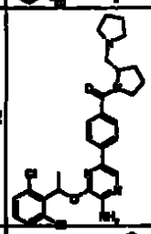
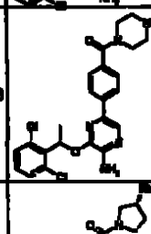
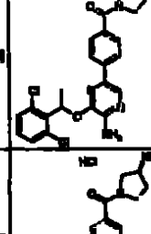
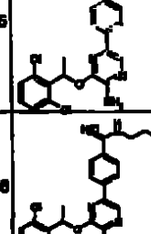
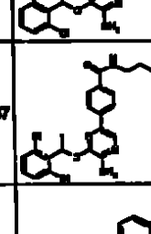
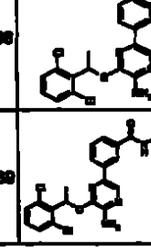
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-124		(3-[5-Amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone	0.23	4 as in Example II-122	(300MHZ, CDCl3) δ 8.10 (s, 1H), 7.90 (m, 2H), 7.60-7.20 (m, 5H), 5.70 (s, 2H), 4.91 (s, 2H), 3.85 (m, 2H), 3.50 (m, 2H), 2.62 (m, 2H), 2.32 (m, 2H), 2.23 (s, 3H).	490
II-125		3-[5-Amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide	0.22	4 as in Example II-122	(300MHZ, CDCl3) δ 8.85 (bm, 1H), 8.34 (s, 1H), 8.13 (s, 1H), 7.85 (d, 1H), 7.80 (d, 1H), 7.58 (m, 1H), 7.45 (m, 2H), 7.20 (t, 1H), 6.72 (s, 2H), 4.92 (s, 2H), 3.81 (m, 2H), 2.72 (m, 2H), 2.57 (m, 4H), 1.82 (m, 2H), 1.78 (m, 4H).	618
II-126		N-[2-(4-Acetyl-piperazin-1-yl)-ethyl]-3-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-benzamide	0.88	4 as in Example II-122	(300MHZ, CDCl3) δ 8.28 (s, 1H), 8.14 (s, 1H), 7.98 (d, 1H), 7.87 (d, 1H), 7.68 (m, 1H), 7.62 (t, 1H), 7.42 (d, 1H), 7.22 (t, 1H), 6.75 (bm, 1H), 5.72 (s, 2H), 4.95 (s, 2H), 3.82 (m, 4H), 3.47 (m, 2H), 2.63 (m, 2H), 2.62 (m, 4H), 2.08 (s, 3H).	591
II-127		(4-[5-Amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.047	4 as in Example II-94	(300MHZ, CDCl3) δ 8.10 (s, 1H), 7.89 (d, 2H), 7.62 (m, 1H), 7.44 (d, 2H), 7.42 (m, 1H), 7.20 (t, 1H), 5.71 (s, 2H), 5.08 (s, 2H), 4.62 (m, 1H), 3.82 (m, 1H), 3.09 (m, 1H), 2.98 (m, 1H), 2.68 (m, 4H), 2.28 (m, 1H), 1.92 (m, 1H), 1.81 (m, 6H), 1.55 (m, 2H).	644
II-128		(4-[5-Amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone	0.18	4 as in Example II-94	(300MHZ, CDCl3) δ 8.09 (s, 1H), 7.88 (d, 2H), 7.55-7.40 (m, 4H), 7.21 (t, 1H), 5.72 (s, 2H), 5.01 (s, 2H), 3.82 (m, 2H), 3.60 (m, 2H), 2.50 (m, 2H), 2.32 (m, 2H), 2.23 (s, 3H).	490
II-129		(4-[5-Amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-phenyl)-([S]-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.092	4 as in Example II-94	(300MHZ, CDCl3) δ 8.11 (s, 1H), 7.88 (d, 2H), 7.68 (m, 3H), 7.42 (d, 1H), 7.22 (t, 1H), 5.72 (s, 2H), 4.92 (s, 2H), 3.80 (m, 2H), 3.74 (m, 1H), 1.84 (d, 3H), 1.57-2.16 (m, 11H).	644
II-130		(3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone	0.17	4 as in Example II-94	(300MHZ, CDCl3) δ 8.02 (s, 1H), 7.79 (m, 2H), 7.49 (t, 1H), 7.29 (m, 1H), 7.01 (t, 1H), 6.81 (q, 1H), 5.06 (s, 2H), 3.85 (m, 2H), 3.48 (m, 2H), 2.61 (m, 2H), 2.38 (m, 2H), 2.33 (s, 3H), 1.84 (d, 3H).	508
II-131		(3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-((2R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone	0.12	4 as in Example II-94	(300MHZ, CDCl3) δ 8.02 (s, 1H), 7.78 (m, 2H), 7.39 (t, 1H), 7.24 (m, 1H), 7.01 (t, 1H), 6.81 (q, 1H), 5.07 (s, 2H), 4.71 (m, 1H), 3.88 (m, 1H), 2.98 (m, 1H), 2.82 (m, 1H), 2.66 (m, 1H), 2.42 (m, 1H), 1.84 (d, 3H), 1.74 (m, 1H), 1.22 (d, 3H), 1.00 (d, 3H).	618
II-132		3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(1-methyl-piperidin-4-yl)-benzamide	0.13	4 as in Example II-94	(300MHZ, CD3OD) δ 8.16 (s, 1H), 7.99 (s, 1H), 7.82 (d, 1H), 7.69 (d, 1H), 7.42 (m, 2H), 7.15 (t, 1H), 6.74 (q, 1H), 3.98 (m, 1H), 2.98 (m, 2H), 2.34 (s, 3H), 2.28 (m, 2H), 2.01 (m, 2H), 1.84 (d, 3H), 1.73 (m, 2H).	620

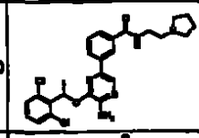
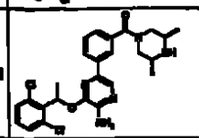
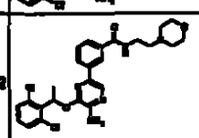
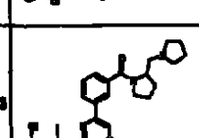
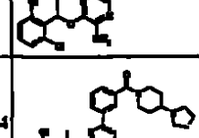
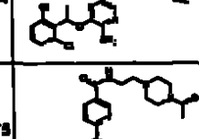
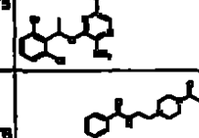
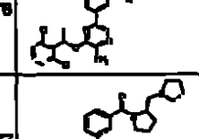
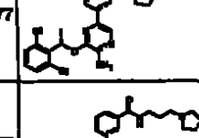
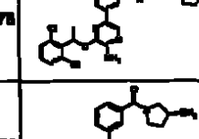
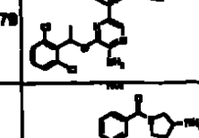
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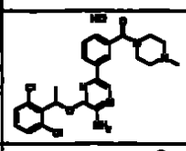
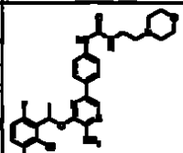
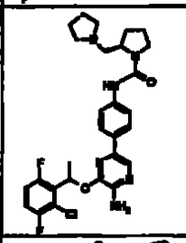
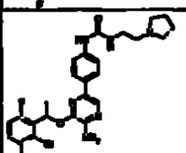
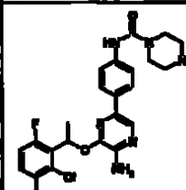
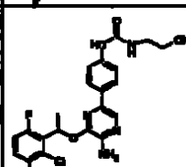
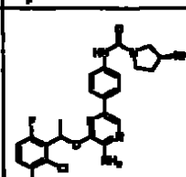
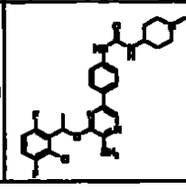
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-133		3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide	0.17	4 as in Example II-84	(300MHZ, CD3OD) δ 8.17 (s, 1H), 7.99 (s, 1H), 7.82 (d, 1H), 7.69 (d, 1H), 7.38 (m, 2H), 7.12 (t, 1H), 6.72 (q, 1H), 3.64 (m, 2H), 2.89 (m, 2H), 2.76 (m, 4H), 2.25 (m, 2H), 2.01 (m,. 2H), 1.84 (m, 7H).	520
II-134		3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide	0.21	4 as in Example II-84	(300MHZ, CDCl3) δ 8.13 (s, 1H), 8.03 (s, 1H), 7.85 (d, 1H), 7.67 (d, 1H), 7.42 (t, 1H), 7.28 (dd, 1H), 7.00 (t, 1H), 6.89 (q, 1H), 6.84 (bm, 1H), 5.11 (s, 2H), 3.72 (m, 4H), 3.61 (m, 2H), 2.63 (m, 2H), 2.53 (m, 4H), 1.84 (d, 3H).	534
II-135		3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(3-morpholin-4-yl-propyl)-benzamide	0.26	4 as in Example II-84	(300MHZ, CDCl3) δ 8.19 (s, 1H), 8.08 (s, 1H), 7.87 (d, 1H), 7.70 (bm,. 1H), 7.67 (d, 1H), 7.42 (t, 1H), 7.28 (dd, 1H), 7.01 (t, 1H), 6.86 (q, 1H), 5.11 (s, 2H), 3.64 (m, 6H), 2.54 (m, 2H), 2.48 (m, 4H), 1.84 (m, 5H).	548
II-136		(3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-(4-cyclopropylamino-piperidin-1-yl)-methanone	0.15	4 as in Example II-84		544
II-137		3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-((S)-2-hydroxy-3-morpholin-4-yl-propyl)-benzamide	0.3	4 as in Example II-84		564
II-138		3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-((R)-2-hydroxy-3-pyrrolidin-1-yl-propyl)-benzamide	0.13	4 as in Example II-84		548
II-139		(3-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.071	4 as in Example II-84	(200MHZ, CDCl3) δ 7.86 (s, 1H), 7.41 (m, 3H), 7.30 (m, 3H), 7.07 (t, 1H), 6.99 (s, 1H), 6.12 (q, 1H), 4.96 (s, 2H), 4.70 (m, 1H), 3.62 (m, 1H), 3.06 (m, 1H), 2.89 (m, 1H), 2.65 (m, 4H), 2.26 (m, 1H), 1.02 (m, 1H), 1.81 (m, 6H), 1.65 (m, 2H).	569
II-140		2-Diethylamino-ethanesulfonic acid (4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-amide	0.35	3 as in Example I-243	(300MHZ, CDCl3) δ 7.89 (s, 1H), 7.70 (d, 2H), 7.28 (m, 2H), 7.21 (d, 2H), 7.01 (t, 1H), 6.82 (q, 1H), 6.05 (s, 2H), 3.22 (m, 2H), 3.00 (m, 2H), 2.85 (m, 4H), 1.83 (d, 3H), 1.80 (d, 6H).	556
II-141		2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid (4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-amide	0.21	3 as in Example I-243	(300MHZ, CDCl3) δ 7.95 (s, 1H), 7.71 (d, 2H), 7.28 (m, 2H), 7.21 (d, 2H), 7.01 (t, 1H), 6.82 (q, 1H), 5.00 (s, 2H), 3.78 (m, 1H), 3.25 (t, 2H), 2.90 (t, 2H), 2.82 (m, 2H), 2.25 (m, 2H), 1.90 (m, 2H), 1.84 (d, 3H), 1.80 (m, 2H).	584
II-142		2-Dimethylamino-ethanesulfonic acid (4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-amide	0.22	3 as in Example I-243	(300MHZ, CDCl3) δ 7.89 (s, 1H), 7.70 (d, 2H), 7.28 (m, 2H), 7.21 (d, 2H), 7.01 (t, 1H), 6.82 (q, 1H), 5.05 (s, 2H), 3.20 (m, 2H), 2.85 (m, 2H), 2.28 (s, 3H), 1.83 (d, 3H).	528

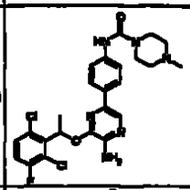
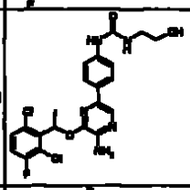
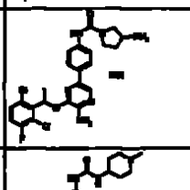
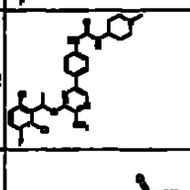
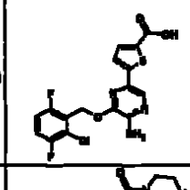
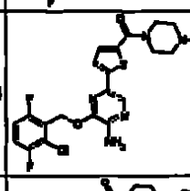
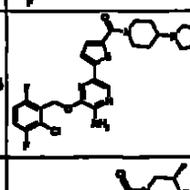
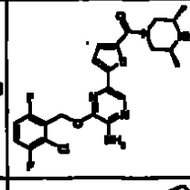
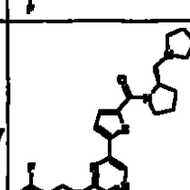
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-143		2-((R)-3-Hydroxy-pyrrolidin-1-yl)-ethanesulfonic acid (4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide	0.19	3 as in Example I-243	(300MHZ, CDCl3) δ 7.93 (s, 1H), 7.89 (d, 2H), 7.27 (m, 4H), 7.00 (t, 1H), 6.84 (q, 1H), 5.03 (s, 2H), 4.43 (m, 1H), 3.28 (m, 2H), 3.02 (m, 3H), 2.84 (m, 1H), 2.63 (m, 1H), 2.30 (m, 1H), 2.22 (m, 1H), 1.84 (d, 3H), 1.61 (m, 1H).	570
II-144		2-Pyrrolidin-1-yl-ethanesulfonic acid (4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide	0.36	3 as in Example I-243	(300MHZ, CDCl3) δ 7.94 (s, 1H), 7.89 (d, 2H), 7.27 (m, 2H), 7.19 (d, 2H), 7.04 (t, 1H), 6.82 (q, 1H), 5.01 (s, 2H), 3.28 (m, 2H), 3.08 (m, 2H), 2.80 (m, 4H), 1.88 (m, 7H).	554
II-145		4-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-benzoic acid	1.56	3 as in Example I-211		422
II-146		4-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-((R)-2-hydroxy-3-pyrrolidin-1-yl-propyl)-benzamide	0.16	4 as in Example II-148		548
II-147		(4-{5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-cyclopropylamino-piperidin-1-yl)-methanone	0.13	4 as in Example II-148		544
II-148		4-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-((S)-2-hydroxy-3-pyrrolidin-1-yl-propyl)-benzamide	0.12	4 as in Example II-148		548
II-149		4-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-((R)-2-hydroxy-3-morpholin-4-yl-propyl)-benzamide	0.13	4 as in Example II-148		564
II-150		4-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(1-methyl-piperidin-4-yl)-benzamide	0.088	4 as in Example II-148	(300MHZ, CDCl3) δ 8.01 (s, 1H), 7.78 (m, 4H), 7.28 (m, 1H), 6.95 (t, 1H), 6.80 (q, 1H), 6.65 (bd, 1H), 6.07 (s, 2H), 4.06 (m, 1H), 2.85 (m, 2H), 2.32 (s, 3H), 2.21 (m, 2H), 2.08 (m, 2H), 1.85 (d, 3H), 1.68 (m, 2H).	518
II-151		(4-{5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.18	4 as in Example II-148	(300MHZ, CDCl3) δ 8.00 (d, 1H), 7.75 (d, 2H), 7.61 (d, 2H), 7.28 (m, 1H), 7.00 (t, 1H), 6.80 (q, 1H), 5.05 (s, 2H), 4.45 (m, 1H), 3.41 (m, 2H), 2.70 (m, 4H), 1.84 (d, 3H), 1.70-2.0 (m, 10H)	558

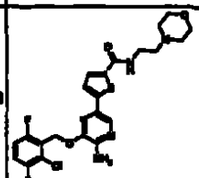
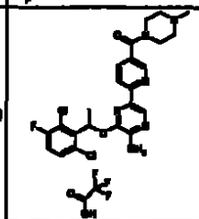
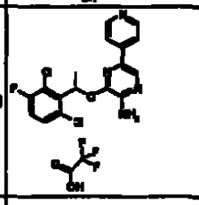
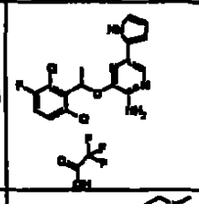
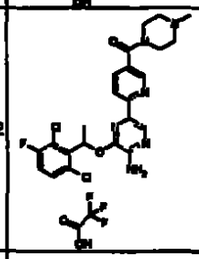
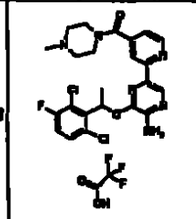
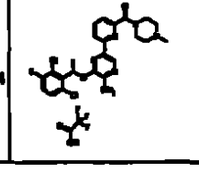
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-152		(4-{5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.11	4 as in Example II-148	(300MHZ, CDCl3) δ 7.00 (s, 1H), 7.76 (d, 2H), 7.40 (d, 2H), 7.28 (m, 1H), 6.99 (t, 1H), 6.76 (q, 1H), 5.04 (s, 2H), 4.64 (m, 1H), 3.84 (m, 1H), 3.02 (m, 2H), 2.80 (m, 4H), 2.30 (m, 1H), 1.92 (m, 1H), 1.81 (m, 8H), 1.59 (m, 2H), 1.82 (m, 2H).	558
II-153		4-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide	0.102	4 as in Example II-148	(300MHZ, CDCl3) δ 8.05 (s, 1H), 7.79 (m, 6H), 7.25 (m, 1H), 6.96 (t, 1H), 6.83 (q, 1H), 5.10 (s, 2H), 3.74 (m, 4H), 3.48 (m, 2H), 2.63 (m, 2H), 2.52 (m, 4H), 1.86 (d, 3H).	536
II-154		(4-{5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone	0.16	4 as in Example II-148	(300MHZ, CDCl3) δ 7.99 (s, 1H), 7.78 (d, 2H), 7.43 (d, 2H), 7.29 (m, 1H), 6.85 (t, 1H), 6.84 (q, 1H), 5.07 (s, 2H), 3.75 (m, 2H), 3.50 (m, 2H), 2.43 (m, 4H), 2.33 (s, 3H), 1.84 (d, 3H).	508
II-155		(4-{5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone	0.095	4 as in Example II-148	(300MHZ, CDCl3) δ 8.02 (s, 1H), 7.79 (d, 2H), 7.40 (d, 2H), 7.28 (m, 1H), 6.98 (t, 1H), 6.84 (q, 1H), 5.04 (s, 2H), 4.58 (m, 1H), 3.58 (m, 1H), 2.88 (m, 2H), 2.70 (m, 1H), 2.44 (m, 1H), 1.84 (d, 3H), 1.65 (m, 1H), 1.13 (m, 3H), 1.00 (m, 3H).	518
II-156		4-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-benzoic acid		3 as in Example I-211		404
II-157		(4-{5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.16	4 as in Example II-157	(300MHZ, CDCl3) δ 8.05 (s, 1H), 7.82 (d, 2H), 7.50 (d, 2H), 7.31 (d, 2H), 7.15 (t, 1H), 6.80 (q, 1H), 5.05 (s, 2H), 2.92 (br, 2H), 2.60 (s, 4H), 2.25 (br, 2H), 1.99 (d, 3H), 1.2-1.98(br, 9H).	540
II-158		4-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide	0.32	4 as in Example II-157	(300MHZ, CDCl3) δ 8.16 (s, 1H), 7.89 (d, 2H), 7.75 (d, 2H), 7.32 (m, 2H), 7.16 (t, 1H), 6.91 (q, 1H), 6.78 (m, 1H), 5.10 (s, 2H), 3.74 (m, 4H), 3.53 (m, 2H), 2.68 (m, 2H), 2.54 (m, 4H), 1.85 (d, 3H).	516
II-159		(4-{5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone	0.14	4 as in Example II-157	(300MHZ, CDCl3) δ 8.05 (s, 1H), 7.82 (d, 2H), 7.50 (d, 2H), 7.31 (d, 2H), 7.15 (t, 1H), 6.80 (q, 1H), 5.05 (s, 2H), 4.60(s, 1H), 4.30(t, 1H), 3.60 (s, 1H), 2.70 (m, 4H), 1.89 (d, 3H), 0.8-1.2(br, 6H).	500
II-160		4-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(1-methyl-piperidin-4-yl)-benzamide	0.12	4 as in Example II-157	(300MHZ, CDCl3) δ 8.16 (s, 1H), 7.90 (d, 2H), 7.63 (d, 2H), 7.32 (t, 2H), 7.16 (t, 1H), 6.84 (q, 1H), 6.00 (d, 1H), 5.08 (s, 2H), 4.06 (m, 1H), 2.81 (m, 2H), 2.38 (s, 3H), 2.21 (m, 2H), 2.08 (m, 2H), 1.84 (d, 3H), 1.60 (m, 2H).	600

No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-161		(4-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-((R)-3-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.16	4 as in Example II-157	(300MHZ, CDCl3) δ 8.05 (s, 1H), 7.82 (d, 2H), 7.50 (d, 2H), 7.28 (d, 2H), 7.15 (t, 1H), 6.90 (s, 1H), 6.05 (s, 2H), 4.30 (t, 1H), 3.50 (m, 2H), 2.65 (m, 4H), 1.88 (d, 3H), 1.70-2.0 (m, 10H)	542
II-162		(4-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-((S)-3-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.14	4 as in Example II-157	(300MHZ, CDCl3) δ 8.05 (s, 1H), 7.82 (d, 2H), 7.50 (d, 2H), 7.31 (d, 2H), 7.15 (t, 1H), 6.90 (s, 1H), 6.05 (s, 2H), 4.45 (m, 1H), 3.41 (m, 2H), 2.70 (m, 4H), 1.88 (d, 3H), 1.70-2.0 (m, 10H)	542
II-163		(4-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone	0.15	4 as in Example II-157	(300MHZ, CDCl3) δ 8.05 (s, 1H), 7.82 (d, 2H), 7.50 (d, 2H), 7.31 (d, 2H), 7.15 (t, 1H), 6.90 (s, 1H), 6.05 (s, 2H), 3.60 (m, 4H), 2.45 (m, 4H), 2.31 (s, 3H), 1.89 (d, 3H)	488
II-164		(4-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-((R)-3-aminopyrrolidin-1-yl)-methanone	0.15	4 as in Example II-157	(300MHZ, CD3OD) δ 7.99 (m, 3H), 7.60 (m, 2H), 7.40 (m, 2H), 7.25 (m, 1H), 6.74 (m, 1H), 4.80(s, 2H), 4.05-3.60 (m, 4H), 3.50 (m, 2H), 2.50 (m, 1H), 2.15 (m, 1H), 1.90 (d, 3H).	472
II-165		(4-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-((S)-3-aminopyrrolidin-1-yl)-methanone hydrogen chloride	0.1	4 as in Example II-157	(300MHZ, CD3OD) δ 7.99 (m, 3H), 7.60 (m, 2H), 7.40 (m, 2H), 7.25 (m, 1H), 6.74 (m, 1H), 4.80(s, 2H), 4.05-3.60 (m, 4H), 3.50 (m, 2H), 2.50 (m, 1H), 2.15 (m, 1H), 1.90 (d, 3H).	472
II-166		4-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide	0.11	4 as in Example II-157	(300MHZ, CDCl3) δ 8.01 (s, 1H), 7.80 (m, 4H), 7.31 (d, 2H), 7.15 (t, 1H), 6.84 (m, 2H), 6.04 (s, 2H), 3.86 (m, 2H), 2.71 (m, 2H), 2.57 (m, 4H), 1.84 (d, 3H), 1.83 (m, 4H).	502
II-167		4-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide	0.22	4 as in Example II-157	(300MHZ, CDCl3) δ 8.80 (s, 1H), 8.10 (s, 1H), 7.80 (m, 4H), 7.21 (d, 2H), 7.16 (t, 1H), 6.84 (s, 1H), 5.04 (s, 2H), 3.85 (m, 2H), 2.71 (m, 2H), 2.57 (m, 4H), 1.84 (m, 4H), 1.83 (d, 3H), 1.81 (m, 2H).	514
II-168		3-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-benzoic acid		3 as in Example I-211		404
II-169		3-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(1-methyl-piperidin-4-yl)-benzamide	0.18	4 as in Example II-169	(300MHZ, CDCl3) δ 8.16 (s, 1H), 8.03 (s, 1H), 7.88 (d, 1H), 7.70 (d, 1H), 7.42 (t, 1H), 7.28 (d, 2H), 7.10 (t, 1H), 6.94 (s, 1H), 6.15 (bd, 1H), 5.08 (s, 2H), 4.06 (m, 1H), 2.91 (m, 2H), 2.35 (s, 3H), 2.21 (m, 2H), 2.09 (m, 2H), 1.84 (d, 3H), 1.68 (m, 2H).	502

No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-170		3-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide	0.33	4 as in Example II-169	(300MHZ, CDCl3) δ 8.15 (s, 1H), 8.02 (s, 1H), 7.85 (d, 1H), 7.71 (d, 1H), 7.40 (t, 1H), 7.28 (d, 2H), 7.10 (m, 2H), 6.90 (q, 1H), 5.10 (s, 2H), 3.84 (m, 2H), 2.80 (m, 2H), 2.64 (m, 4H), 1.85 (m, 7H).	500
II-171		(3-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone	0.36	4 as in Example II-169	(300MHZ, CDCl3) δ 8.04 (s, 1H), 7.79 (m, 2H), 7.40 (t, 1H), 7.28 (m, 3H), 7.11 (t, 1H), 6.88 (q, 1H), 5.05 (s, 2H), 4.69 (m, 1H), 3.88 (m, 1H), 2.95 (m, 1H), 2.79 (m, 1H), 2.71 (m, 1H), 2.44 (m, 1H), 1.84 (d, 3H), 1.25 (d, 3H), 1.17 (d, 3H).	500
II-172		3-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide	0.46	4 as in Example II-169	(300MHZ, CDCl3) δ 8.16 (s, 1H), 8.03 (s, 1H), 7.89 (d, 1H), 7.69 (d, 1H), 7.43 (t, 1H), 7.28 (d, 2H), 7.10 (t, 1H), 6.91 (q, 1H), 6.66 (m, 1H), 5.10 (s, 2H), 3.74 (m, 4H), 3.63 (m, 2H), 2.65 (m, 2H), 2.54 (m, 4H), 1.85 (d, 3H).	516
II-173		(3-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.18	4 as in Example II-169	(300MHZ, CDCl3) δ 8.01 (d, 1H), 7.87 (m, 2H), 7.37 (m, 2H), 7.28 (m, 2H), 7.11 (t, 1H), 6.90 (m, 1H), 5.05 (s, 2H), 4.45 (m, 1H), 3.41 (m, 2H), 2.70 (m, 4H), 1.84 (d, 3H), 1.70-2.0 (m, 10H)	540
II-174		(3-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.17	4 as in Example II-169	(300MHZ, CDCl3) δ 7.99 (s, 1H), 7.78 (m, 2H), 7.39 (t, 1H), 7.29 (m, 3H), 7.08 (t, 1H), 6.87 (q, 1H), 5.04 (s, 2H), 4.64 (m, 1H), 3.94 (m, 1H), 3.02 (m, 2H), 2.60 (m, 4H), 2.30 (m, 1H), 1.92 (m, 1H), 1.81 (m, 6H), 1.69 (m, 2H), 1.62 (m, 2H).	540
II-175		N-[2-(4-Acetyl-piperazin-1-yl)-ethyl]-4-[5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-benzamide	0.29	4 as in Example II-169	(300MHZ, CDCl3) δ 8.06(s, 1H), 7.89 (d, 2H), 7.75 (d, 2H), 7.31 (dt, 2H), 7.11 (t, 1H), 6.91 (q, 1H), 6.78 (m, 1H), 5.12 (s, 2H), 4.25 (t, 1H), 3.60 (m, 3H), 3.46 (m, 1H), 2.65 (t, 2H), 2.50 (m, 3H), 2.05(s, 2H),1.85 (d, 3H).	559
II-176		N-[2-(4-Acetyl-piperazin-1-yl)-ethyl]-3-[5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-benzamide	0.35	4 as in Example II-169	(300MHZ, CDCl3) δ 8.16 (s, 1H), 8.03 (s, 1H), 7.89 (d, 1H), 7.69 (d, 1H), 7.43 (t, 1H), 7.28 (d, 2H), 7.11 (t, 1H), 6.91 (q, 1H), 6.78 (m, 1H), 5.12 (s, 2H), 3.66 (m, 4H), 3.49 (m, 2H), 2.68 (m, 2H), 2.61 (m, 4H), 2.09 (s, 3H), 1.85 (d, 3H).	559
II-177		(3-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.33	4 as in Example II-169	(300MHZ, CDCl3) δ 8.01 (d, 1H), 7.87 (m, 2H), 7.37 (m, 2H), 7.28 (m, 2H), 7.11 (t, 1H), 6.90 (m, 1H), 5.05 (s, 2H), 4.45 (m, 1H), 3.41 (m, 2H), 2.70 (m, 4H), 1.84 (d, 3H), 1.70-2.0 (m, 10H)	540
II-178		3-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide	0.34	4 as in Example II-169	(300MHZ, CDCl3) δ 8.46 (m, 1H), 8.22 (t, 1H), 8.05 (s, 1H), 7.91 (dt, 1H), 7.66 (d, 1H), 7.40 (t, 1H), 7.28 (d, 2H), 7.10 (t, 1H), 6.84 (q, 1H), 5.04 (s, 2H), 3.62 (m, 2H), 2.71 (m, 2H), 2.67 (m, 4H), 1.84 (d, 3H), 1.83 (m, 2H), 1.81 (m, 4H).	514
II-179		(3-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone	0.11	4 as in Example II-169	(300MHZ, CD3OD) δ 7.83 (m, 3H), 7.48 (m, 2H), 7.37 (m, 2H), 7.23 (m, 1H), 6.74 (m, 1H), 4.05-3.80 (m, 4H), 3.50 (m, 1H), 2.50 (m, 1H), 2.18 (m, 1H), 1.90 (d, 3H).	472
II-180		(3-[5-Amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone hydrochloride salt	0.18	4 as in Example II-169	(300MHZ, CD3OD) δ 7.83 (m, 3H), 7.48 (m, 2H), 7.37 (m, 2H), 7.23 (m, 1H), 6.74 (m, 1H), 4.05-3.80 (m, 4H), 3.50 (m, 1H), 2.50 (m, 1H), 2.18 (m, 1H), 1.90 (d, 3H).	472

No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-181		(3-{6-Amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone	0.25	4 as in Example II-168	(300MHZ, CDCl3) δ 8.00 (s, 1H), 7.80 (m, 2H), 7.40 (t, 1H), 7.25 (m, 3H), 7.11 (t, 1H), 6.87 (q, 1H), 5.05 (s, 2H), 4.64 (m, 1H), 3.57 (m, 2H), 3.45 (m, 2H), 2.53 (m, 2H), 2.38 (m, 1H), 2.34 (s, 3H), 1.84 (d, 3H).	488
II-182		1-(4-{6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-3-(2-morpholin-4-yl-ethyl)-urea	0.18	10 as in Example II-371	(300MHZ, CDCl3) δ 7.83 (s, 1H), 7.68 (d, 2H), 7.38 (s, 2H), 6.85 (m, 4H), 6.70 (q, 1H), 4.94 (s, 2H), 3.78 (m, 4H), 3.48 (m, 2H), 2.69 (m, 4H), 2.25 (m, 2H), 1.85 (d, 3H).	534
II-183		(R)-2-Pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide	0.21	10 as in Example II-371	(300MHZ, CDCl3) δ 7.83 (s, 1H), 7.40 (d, 2H), 7.27 (d, 2H), 6.85 (m, 3H), 5.95 (q, 1H), 4.85 (s, 2H), 3.85 (m, 1H), 3.75 (m, 1H), 3.40 (m, 1H), 2.90 (m, 4H), 2.83 (m, 4H), 2.10 (m, 3H), 1.85 (d, 3H), 1.9-1.7 (m, 3H).	557
II-184		1-(4-{6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-3-(2-pyrrolidin-1-yl-ethyl)-urea	0.18	10 as in Example II-371	(300MHZ, CDCl3) δ 7.91 (s, 1H), 7.80(bs, 1H), 7.69 (d, 2H), 7.45 (d, 2H), 7.36 (bm, 1H), 7.05 (m, 2H), 6.72 (q, 1H), 4.88 (s, 2H), 3.58 (m, 2H), 3.19 (m, 4H), 3.12 (m, 2H), 2.16 (m, 4H), 2.81 (s, 3H), 1.81 (d, 3H).	517
II-185		4-Methyl-piperazine-1-carboxylic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide	0.1	10 as in Example II-371	(300MHZ, CDCl3) δ 7.96 (s, 1H), 7.69 (d, 2H), 7.39 (d, 2H), 7.01-6.91 (m, 2H), 6.70 (m, 2H), 4.80 (s, 2H), 3.61 (m, 4H), 2.68 (m, 4H), 2.41 (s, 3H), 1.81 (d, 3H).	503
II-186		1-(4-{6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-3-(2-hydroxy-ethyl)-urea	0.21	10 as in Example II-371	(300MHZ, CDCl3) δ 7.78 (s, 1H), 7.60 (d, 2H), 7.35 (d, 2H), 7.15 (m, 4H), 6.95 (q, 1H), 4.86 (s, 2H), 3.64 (t, 2H), 3.31 (t, 3H), 1.82 (d, 3H).	464
II-187		(S)-3-Amino-pyrrolidine-1-carboxylic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide	0.062	10 as in Example II-371	(300MHZ, CDCl3) δ 7.71 (s, 1H), 7.65 (d, 2H), 7.53 (d, 2H), 7.15 (m, 3H), 6.77 (m, 1H), 4.87 (s, 2H), 3.95 (m, 1H), 3.80 (m, 1H), 3.65 (m, 2H), 3.31 (m, 2H), 2.87 (m, 1H), 2.20 (m, 1H), 1.95 (d, 3H).	489
II-188		1-(4-{6-Amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-3-(1-methyl-piperidin-4-yl)-urea	0.054	10 as in Example II-371		517

No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-189		4-Methyl-piperazine-1-carboxylic acid (4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-amide	0.074	10 as in Example I-371	(300MHZ, CDCl3) δ 7.94 (s, 1H), 7.66 (d, 2H), 7.37 (d, 2H), 7.24 (m, 1H), 6.95 (t, 1H), 6.81 (m, 2H), 4.95 (s, 2H), 3.68 (m, 4H), 2.73 (m, 4H), 2.61 (s, 3H), 1.83 (d, 3H).	519
II-190		1-(4-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-3-(2-hydroxy-ethyl)-urea	0.26	10 as in Example I-371	(300MHZ, CDCl3) δ 7.84 (s, 1H), 7.60 (m, 4H), 7.33 (m, 3H), 7.15 (m, 1H), 6.70 (q, 1H), 4.88 (s, 2H), 3.84 (t, 2H), 3.31 (m, 3H), 1.82 (d, 3H).	480
II-191		(S)-3-Amino-pyrrolidine-1-carboxylic acid (4-[5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-amide	3	10 as in Example I-371		502
II-192		1-(4-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-phenyl)-3-(1-methyl-piperidin-4-yl)-urea	0.052	10 as in Example I-371		535
II-193		5-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophene-2-carboxylic acid		3 as in Example I-270		398
II-194		(5-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophen-2-yl)-(4-methyl-piperazin-1-yl)-methanone	0.02	4 as in Example II-19-i	(300MHZ, CDCl3) δ 8.01 (s, 1H), 7.35 (s, 1H), 7.27 (s, 1H), 7.15 (m, 1H), 6.96 (m, 1H), 5.63 (s, 1H), 4.87 (m, 1H), 3.60 (m, 4H), 2.48 (m, 4H), 2.34 (s, 3H).	480
II-195		(5-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophen-2-yl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone	0.51	4 as in Example II-194	(300MHZ, CDCl3) δ 8.01 (s, 1H), 7.35 (d, 1H), 7.24 (d, 1H), 7.15 (m, 1H), 6.96 (m, 1H), 5.63 (s, 2H), 4.88 (m, 2H), 4.42 (m, 4H), 3.06 (t, 4H), 2.63 (m, 2H), 2.35 (m, 1H), 2.00 (m, 2H), 1.82 (m, 2H), 1.80 (m, 2H).	634
II-196		(5-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophen-2-yl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone	0.55	4 as in Example II-194	(300MHZ, CDCl3) δ 8.01 (s, 1H), 7.35 (d, 1H), 7.24 (d, 1H), 7.07 (m, 1H), 7.01 (m, 1H), 5.63 (s, 2H), 4.88 (m, 2H), 4.35 (m, 2H), 2.93 (m, 2H), 2.60 (m, 2H), 1.10 (d, 6H).	494
II-197		(5-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophen-2-yl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone	0.8	4 as in Example II-194	(300MHZ, CDCl3) δ 8.03 (s, 1H), 7.62 (d, 1H), 7.36 (d, 1H), 7.07 (m, 1H), 7.01 (m, 1H), 5.63 (s, 2H), 4.88 (m, 2H), 4.5-0.80 (m, 17H).	634

No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-199		5-[5-Amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophene-2-carboxylic acid (2-morpholin-4-yl-ethyl)-amide	0.7	4 as in Example II-194	(300MHZ, CDCl3) δ 8.03 (s, 1H), 7.45 (d, 1H), 7.38 (d, 1H), 7.20 (m, 1H), 7.05 (m, 1H), 6.88 (m, 1H), 5.68 (s, 2H), 4.89 (m, 2H), 3.75 (m, 4H), 3.55 (m, 2H), 2.61 (m, 2H), 2.50 (m, 4H)	510
II-198		3-[1-(2,6-dichloro-3-fluorophenyl)ethoxy]-5-[5-[(4-methylpiperazin-1-yl)carbonyl]pyridin-2-yl]pyrazin-2-amine trifluoroacetate	0.15	4 as in Example II-194	(DMSO-d6+TFA /300 MHz) δ 8.64 (s, 1H), 8.29 (s, 1H), 7.99 (d, 1H), 7.81 (d, 1H), 7.51 (m, 1H), 7.35 (m, 1H), 6.62 (q, 1H), 4.69-4.25 (m, 1H), 4.08-3.89 (m, 1H), 3.58-3.01 (m, 6H), 2.82 (s, 3H), 1.84 (d, 3H).	505
II-200		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-pyridin-4-yl-pyrazin-2-ylamine	0.048	3		379
II-201		3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(1H-pyrrol-2-yl)-pyrazin-2-ylamine	0.22	3		367
II-202		(6-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-pyridin-3-yl)-(4-methyl-piperazin-1-yl)-methanone	0.15	16 as in Example I-499		505
II-203		(2-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-pyridin-4-yl)-(4-methyl-piperazin-1-yl)-methanone	0.18	16 as in Example I-499	(DMSO-d6+TFA /300 MHz) δ 8.65 (d, 1H), 8.34 (s, 1H), 7.82 (s, 1H), 7.62-7.27 (m, 3H), 6.57 (q, 1H), 4.66 (m, 1H), 3.70-2.91 (m, 7H), 2.89 (s, 3H), 1.82 (d, 3H).	505
II-204		(6-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-pyridin-2-yl)-(4-methyl-piperazin-1-yl)-methanone	0.22	16 as in Example I-499	(DMSO-d6+TFA /300 MHz) δ 8.24 (s, 1H), 7.98 (dd, 1H), 7.78 (d, 1H), 7.53 (m, 2H), 7.35 (dd, 1H), 6.61 (q, 1H), 4.60 (br, 1H), 4.12 (br, 1H), 3.61-3.30 (m, 3H), 3.24-3.04 (m, 3H), 2.83 (s, 3H), 1.84 (d, 3H).	505

130

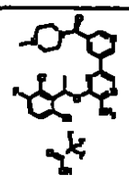
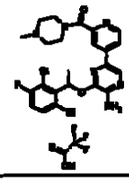
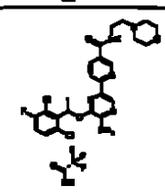
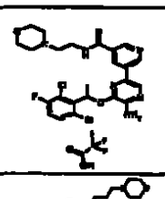
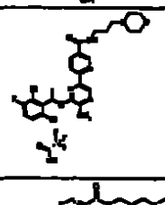
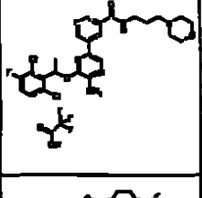
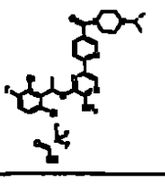
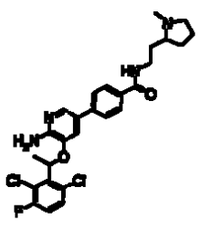
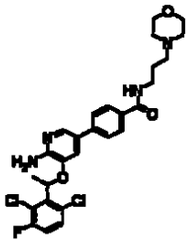
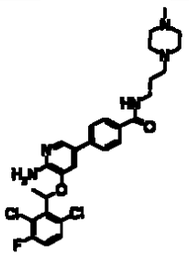
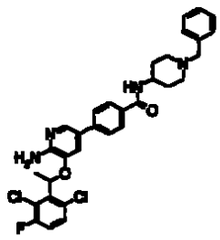
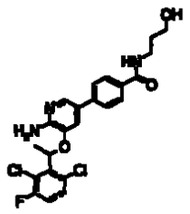
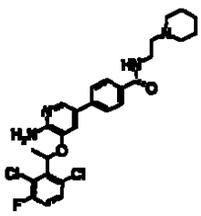
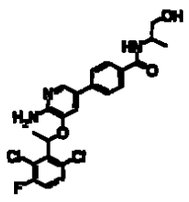
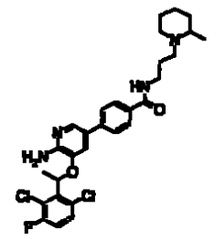
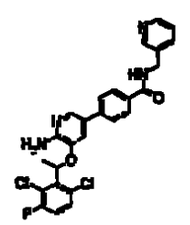
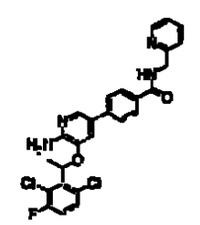
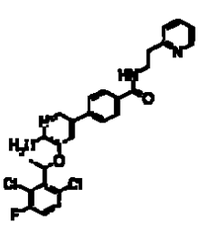
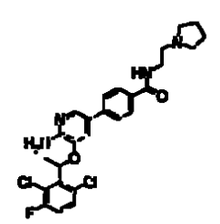
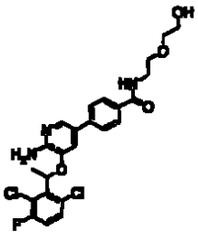
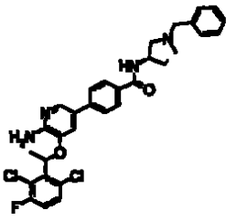
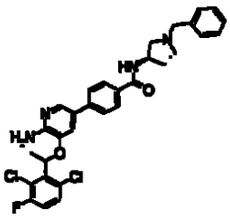
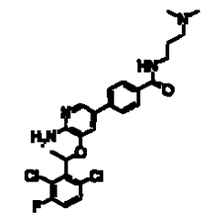
No.	Structure	Name	Met IC_{50} (μM)	Procedure	^{1}H-NMR	MS m/z (M+1)
II-205		(5-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-pyridin-3-yl)-(4-methyl-piperazin-1-yl)-methanone	0.1	16 as in Example I-488	(DMSO-d6+TFA /300 MHz) δ 9.07 (s, 1H), 8.77 (s, 1H), 8.44 (s, 1H), 8.31 (s, 1H), 7.53 (br, 1H), 7.44 (m, 1H), 7.32 (m, 1H), 6.58 (q, 1H), 4.83 (br, 1H), 3.74 (br, 1H), 3.61-3.15 (m, 4H), 3.06 (m, 2H), 2.83 (s, 3H), 1.81 (d, 3H).	505
II-206		(4-(5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl)-pyridin-2-yl)-(4-methyl-piperazin-1-yl)-methanone	0.1	16 as in Example I-488	(DMSO-d6+TFA /300 MHz) δ 8.83 (d, 1H), 8.39 (s, 1H), 8.01 (s, 1H), 7.83 (d, 1H), 7.43 (m, 1H), 7.29 (dd, 1H), 6.68 (q, 1H), 4.83 (m, 1H), 3.92 (m, 1H), 3.84-3.13 (m, 4H), 3.11-2.99 (m, 2H), 2.84 (s, 3H), 1.81 (d, 3H).	505
II-207		6-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(2-morpholin-4-yl-ethyl)-nicotinamide		16 as in Example I-488	(DMSO-d6+TFA /300 MHz) δ 9.76 (br, 1H), 8.96 (m, 2H), 8.57 (s, 1H), 8.28 (d, 1H), 7.80 (d, 1H), 7.51 (m, 1H), 7.37 (dd, 1H), 6.61 (q, 1H), 4.00 (d, 2H), 3.74-3.60 (m, 6H), 3.34 (m, 2H), 3.16 (m, 2H), 1.83 (d, 3H).	535
II-208		6-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(2-morpholin-4-yl-ethyl)-nicotinamide	0.035	16 as in Example I-488	(DMSO-d6+TFA /300 MHz) δ 9.16 (m, 1H), 9.08 (s, 1H), 9.03 (s, 1H), 8.83 (s, 1H), 8.28 (s, 1H), 7.47 (m, 1H), 7.32 (dd, 1H), 6.66 (q, 1H), 4.00 (d, 2H), 3.77-3.50 (m, 6H), 3.35 (m, 2H), 3.16 (m, 2H), 1.85 (d, 3H).	535
II-209		6-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(3-morpholin-4-yl-propyl)-nicotinamide		16 as in Example I-488	(DMSO-d6+TFA /300 MHz) δ 9.74 (br, 1H), 8.97 (s, 1H), 8.84 (m, 1H), 8.36 (s, 1H), 8.28 (d, 1H), 7.79 (d, 1H), 7.50 (m, 1H), 7.37 (dd, 1H), 6.61 (q, 1H), 3.97 (d, 2H), 3.84 (t, 2H), 3.50-3.30 (m, 4H), 3.23-2.98 (m, 4H), 1.92 (m, 2H), 1.83 (d, 3H).	549
II-210		5-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-N-(3-morpholin-4-yl-propyl)-nicotinamide	0.022	16 as in Example I-488	(DMSO-d6+TFA /300 MHz) δ 9.68 (br, 1H), 8.88 (s, 1H), 8.30 (s, 1H), 7.65-7.40 (m, 2H), 7.32 (m, 1H), 6.67 (q, 1H), 3.97 (d, 2H), 3.86 (t, 2H), 3.43 (m, 4H), 3.25-2.97 (m, 4H), 1.98 (br, 2H), 1.83 (d, 3H).	549
II-211		(5-[5-Amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl]-pyridin-3-yl)-(4-isopropyl-piperazin-1-yl)-methanone		16 as in Example I-488	(DMSO-d6+TFA /300 MHz) δ 9.70 (br, 1H), 8.85 (s, 1H), 8.38 (s, 1H), 7.95 (d, 1H), 7.80 (d, 1H), 7.53 (m, 1H) 7.38 (dd, 1H), 6.62 (q, 1H), 4.57 (br, 1H), 3.88 (br, 1H), 3.60-3.05 (m, 7H), 1.83 (d, 3H), 1.28 (d, 6H).	533

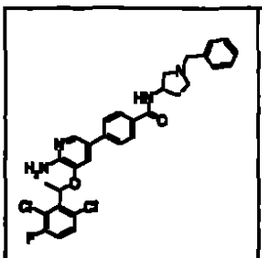
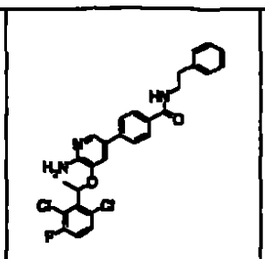
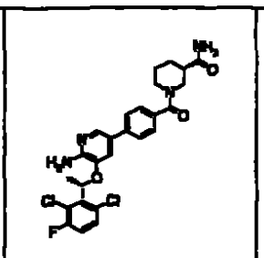
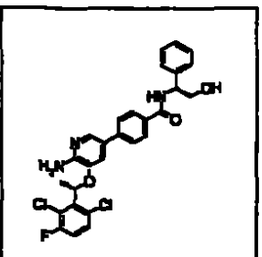
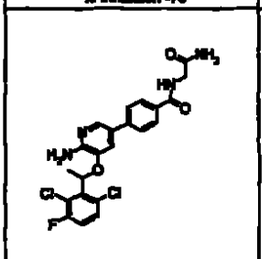
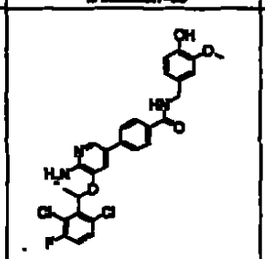
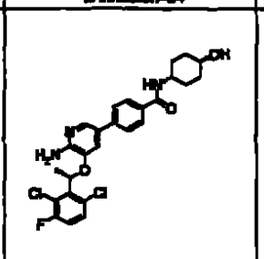
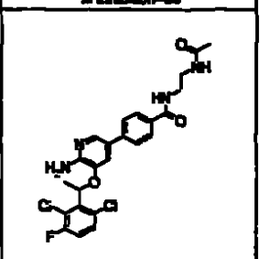
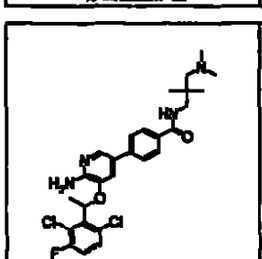
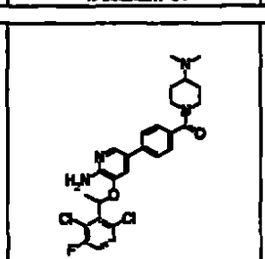
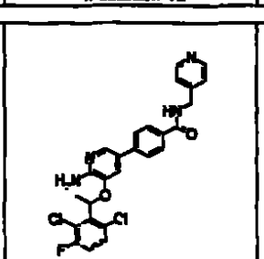
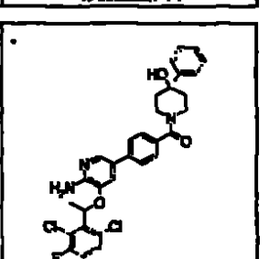
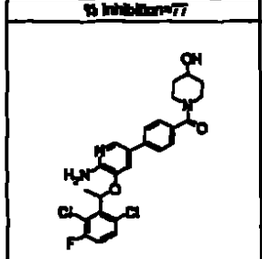
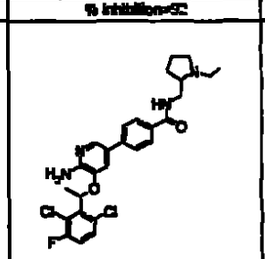
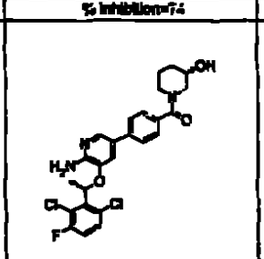
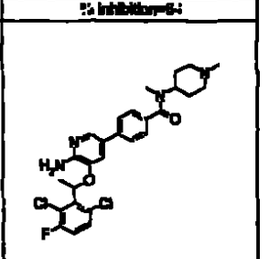
Table 5

Section A: Examples L-1 to L-16

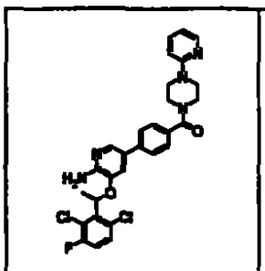
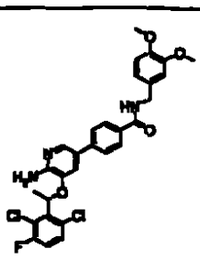
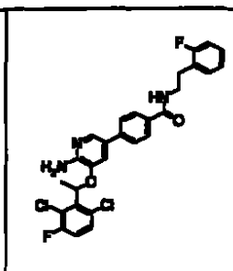
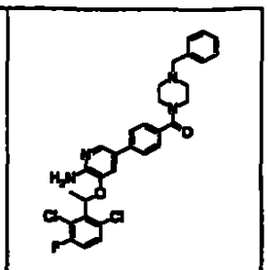
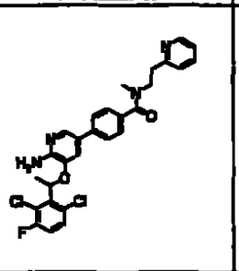
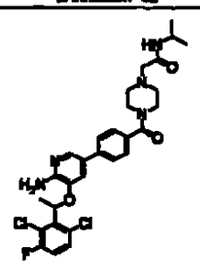
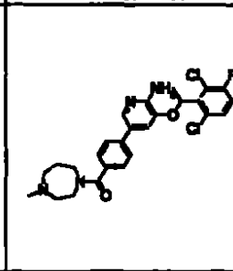
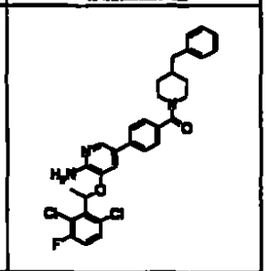
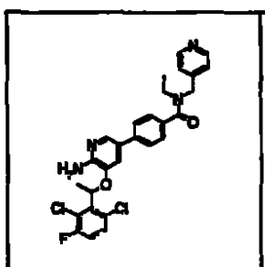
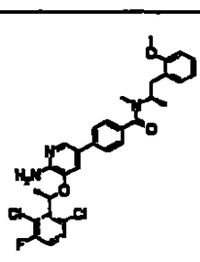
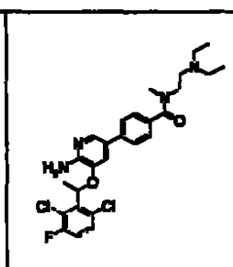
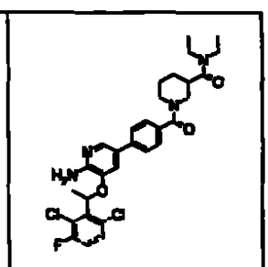
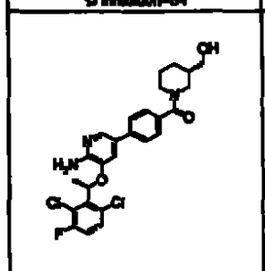
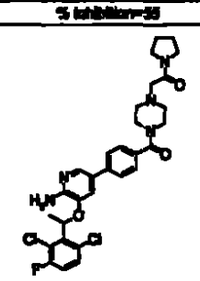
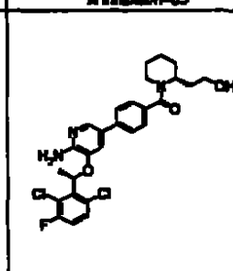
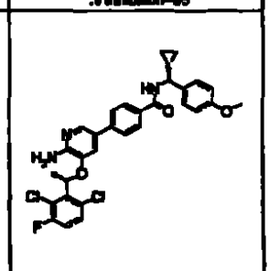
			
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% Inhibition=68	% Inhibition=69	% Inhibition=66	% Inhibition=72
			
% Inhibition=84	% Inhibition=67	% Inhibition=67	% Inhibition=62
			
% Inhibition=78	% Inhibition=72	% Inhibition=67	% Inhibition=63

131

Section B: Examples L-17 to L-32

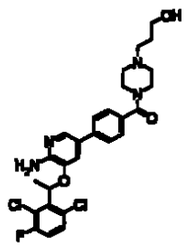
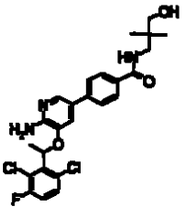
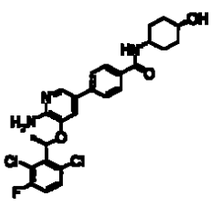
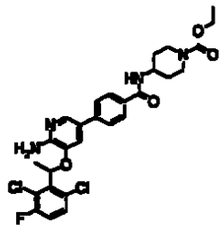
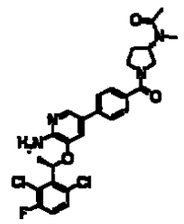
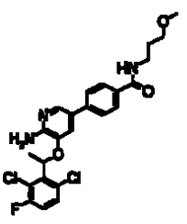
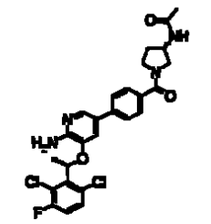
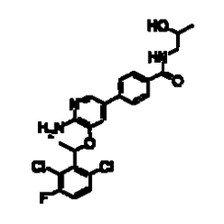
			
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% Inhibition=88	% Inhibition=84	% Inhibition=72	% Inhibition=71
			
% Inhibition=77	% Inhibition=92	% Inhibition=74	% Inhibition=84
			
% Inhibition=88	% Inhibition=80	% Inhibition=85	% Inhibition=92

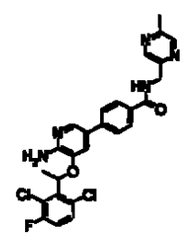
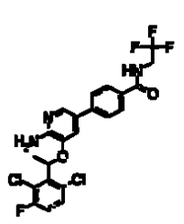
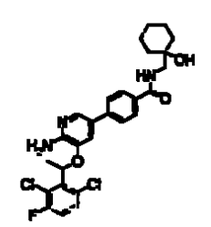
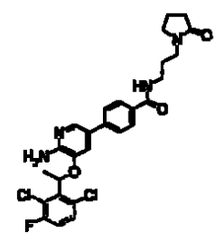
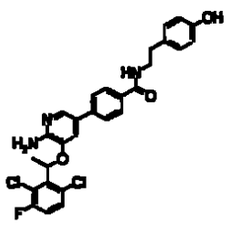
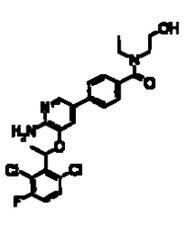
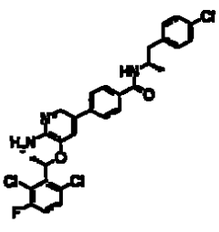
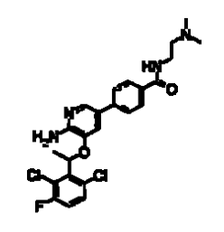
Section C: Examples L-33 to L-48

			
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% Inhibition=78	% Inhibition=86	% Inhibition=77	% Inhibition=85
			
% Inhibition=84	% Inhibition=85	% Inhibition=85	% Inhibition=85
			
% Inhibition=84	% Inhibition=78	% Inhibition=83	% Inhibition=87

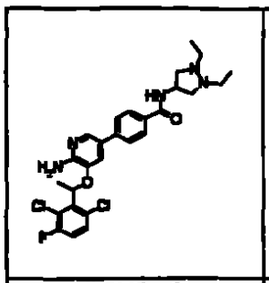
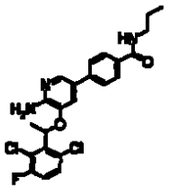
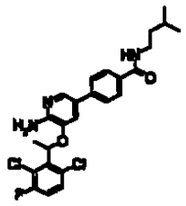
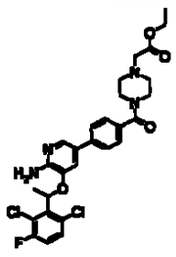
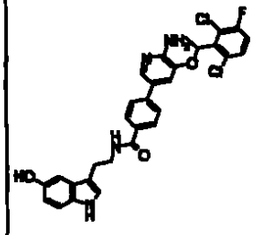
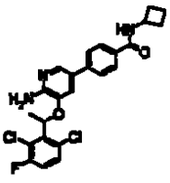
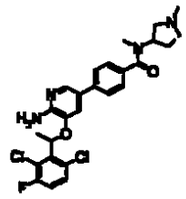
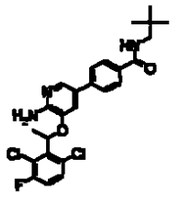
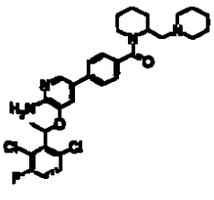
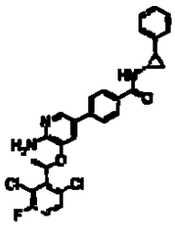
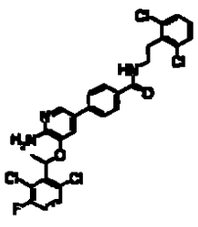
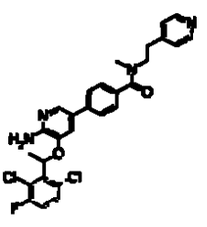
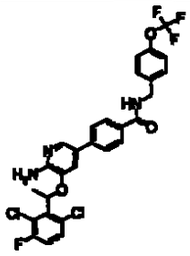
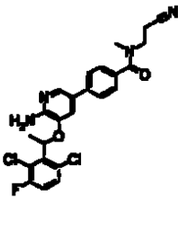
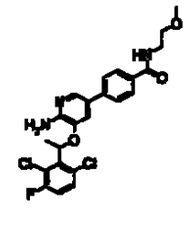
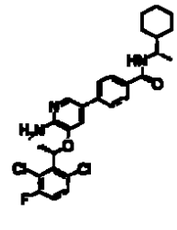
132

Section D: Examples L-49 to L-64

			
% Inhibition=74	% Inhibition=73	% Inhibition=73	% Inhibition=68
			
% Inhibition=70	% Inhibition=65	% Inhibition=77	% Inhibition=63

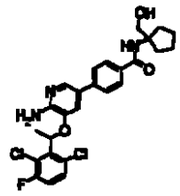
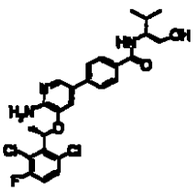
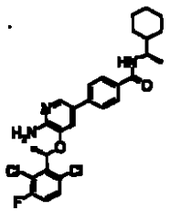
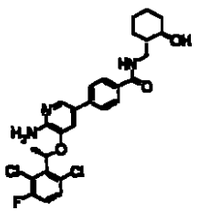
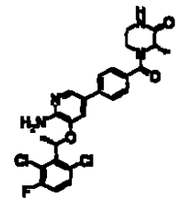
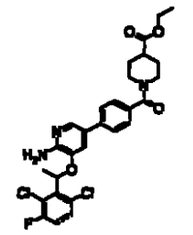
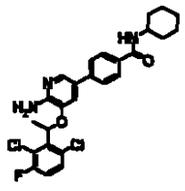
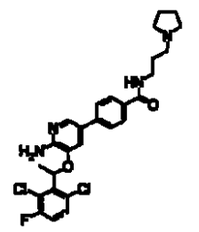
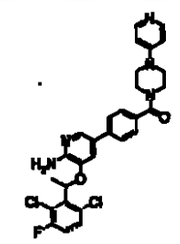
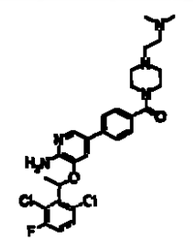
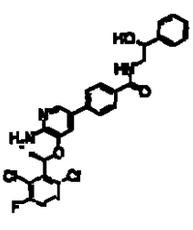
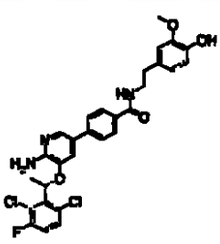
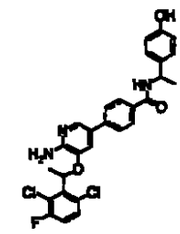
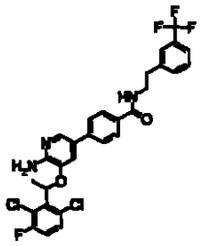
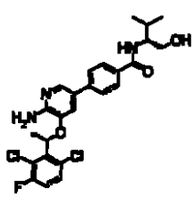
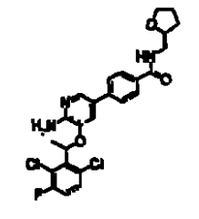
			
% Inhibition=76	% Inhibition=78	% Inhibition=81	% Inhibition=63
			
% Inhibition=71	% Inhibition=84	% Inhibition=68	% Inhibition=69

Section E: Examples L-65 to L-80

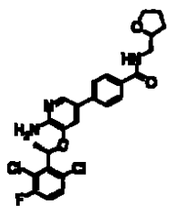
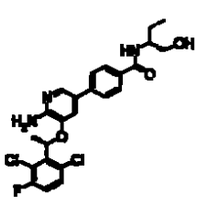
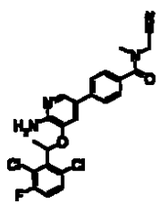
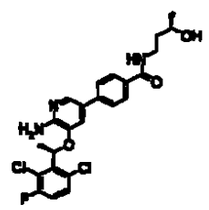
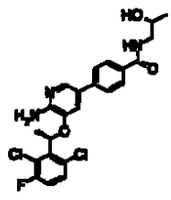
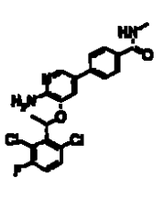
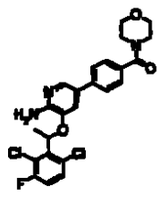
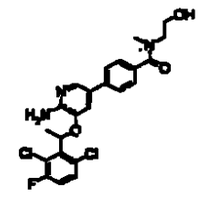
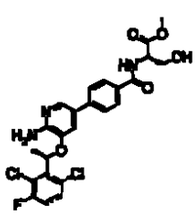
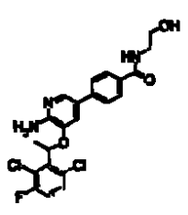
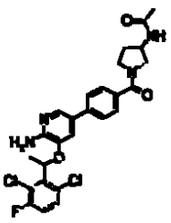
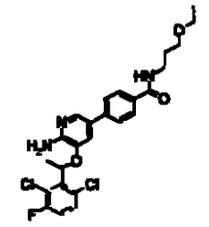
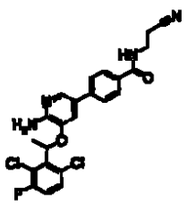
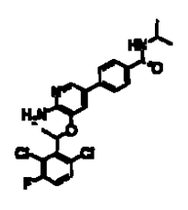
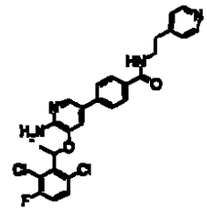
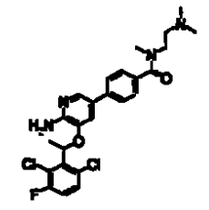
			
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% Inhibition=68	% Inhibition=71	% Inhibition=82	% Inhibition=62
			
% Inhibition=80	% Inhibition=66	% Inhibition=83	% Inhibition=73
			
% Inhibition=84	% Inhibition=68	% Inhibition=73	% Inhibition=80

133

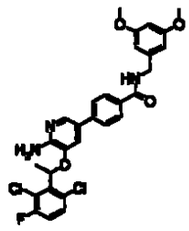
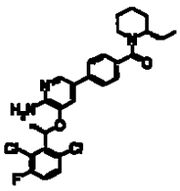
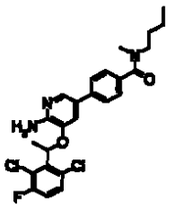
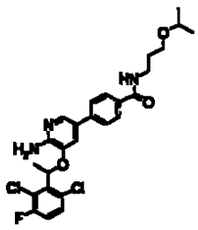
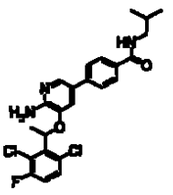
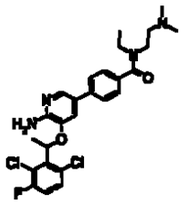
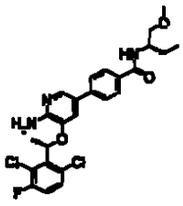
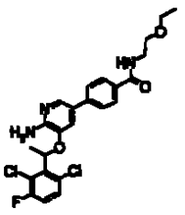
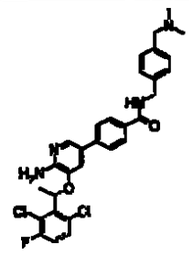
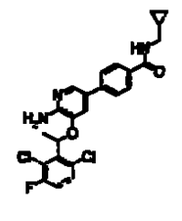
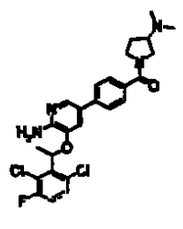
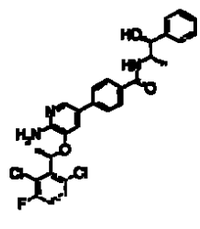
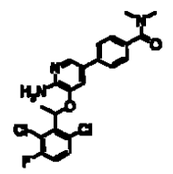
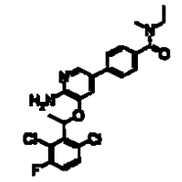
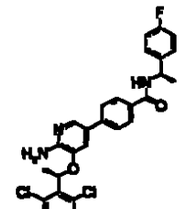
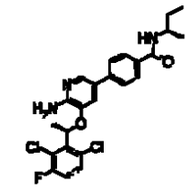
Section F: Examples L-81 to L-88

			
% Inhibition=87	% Inhibition=74	% Inhibition=64	% Inhibition=87
			
% Inhibition=88	% Inhibition=87	% Inhibition=58	% Inhibition=80
			
% Inhibition=86	% Inhibition=85	% Inhibition=69	% Inhibition=64
			
% Inhibition=62	% Inhibition=51	% Inhibition=66	% Inhibition=61

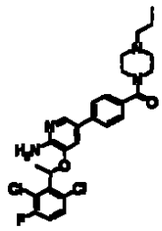
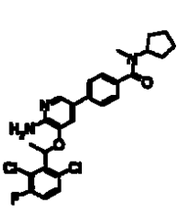
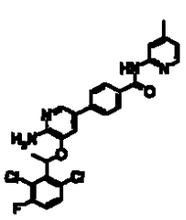
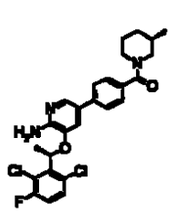
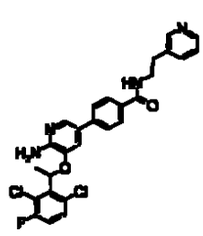
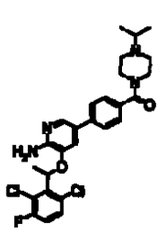
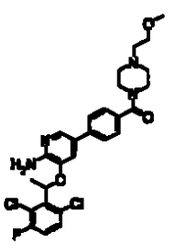
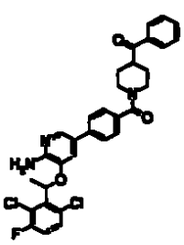
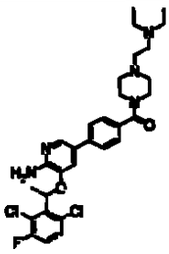
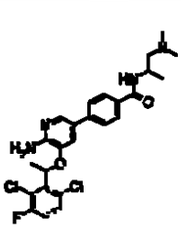
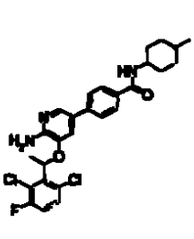
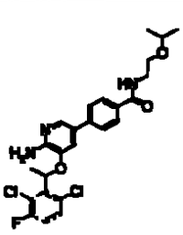
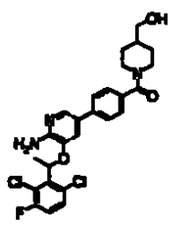
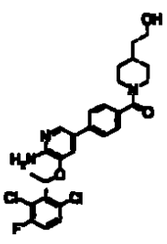
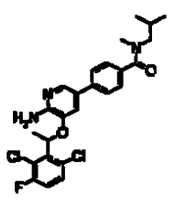
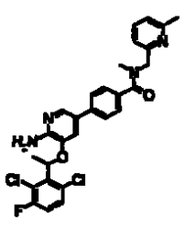
Section G: Examples L-97 to L-112

			
% Inhibition=80	% Inhibition=73	% Inhibition=83	% Inhibition=77
			
% Inhibition=79	% Inhibition=82	% Inhibition=81	% Inhibition=68
			
% Inhibition=81	% Inhibition=69	% Inhibition=67	% Inhibition=70
			
% Inhibition=76	% Inhibition=71	% Inhibition=71	% Inhibition=65

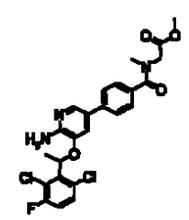
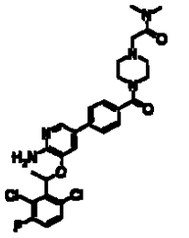
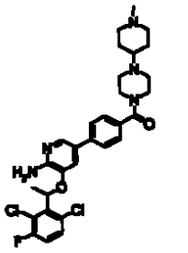
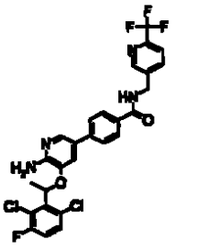
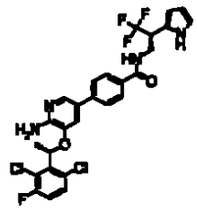
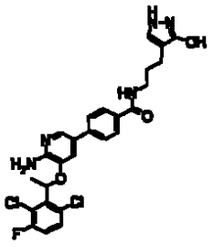
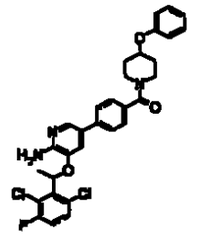
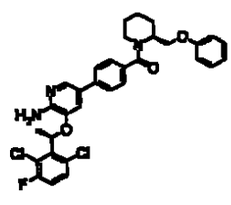
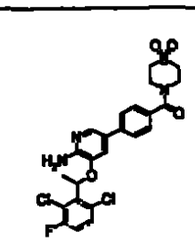
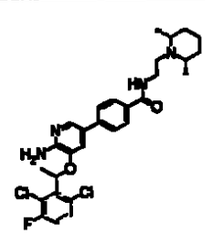
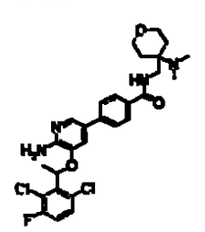
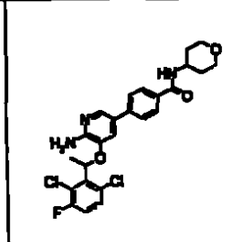
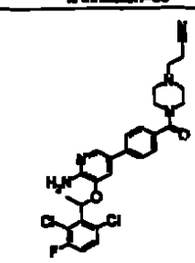
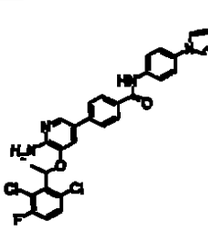
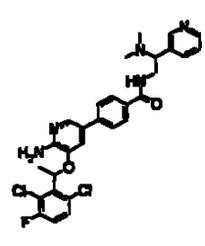
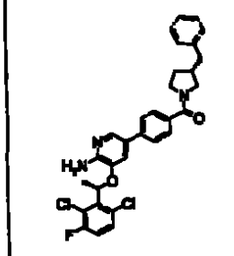
Section H: Examples L-113 to L-128

			
% Inhibition=87	% Inhibition=86	% Inhibition=83	% Inhibition=82
			
% Inhibition=80	% Inhibition=66	% Inhibition=59	% Inhibition=63
			
% Inhibition=75	% Inhibition=61	% Inhibition=60	% Inhibition=69
			
% Inhibition=77	% Inhibition=62	% Inhibition=56	% Inhibition=64

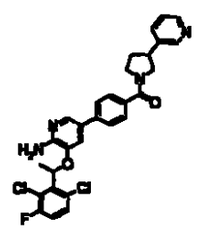
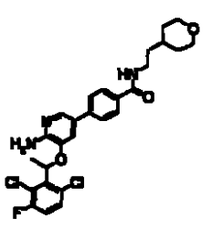
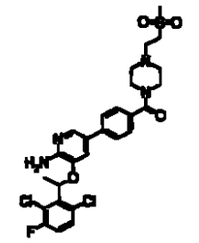
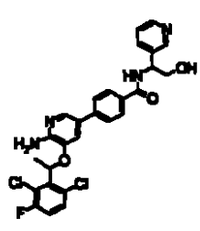
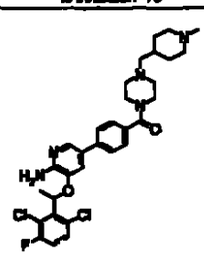
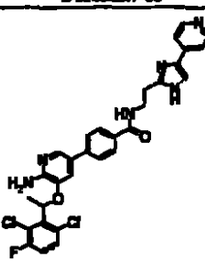
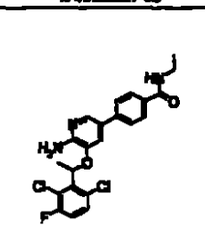
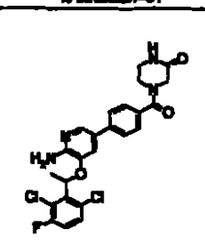
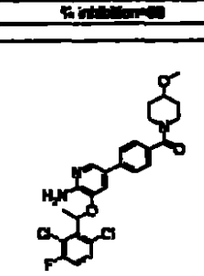
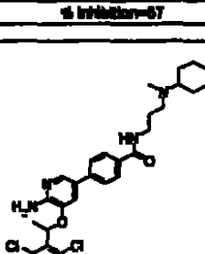
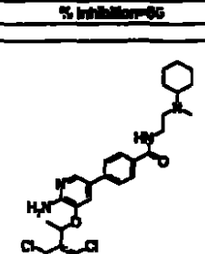
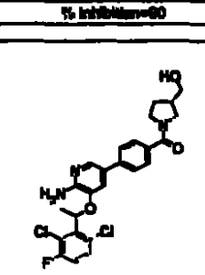
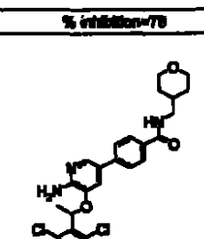
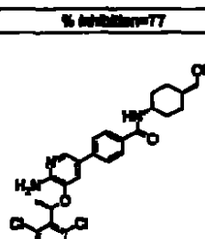
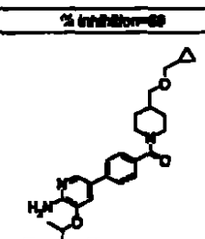
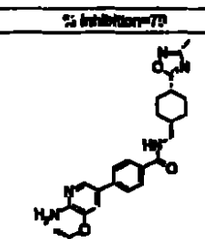
Section I: Examples L-129 to L-144

			
% Inhibition=82	% Inhibition=80	% Inhibition=81	% Inhibition=66
			
% Inhibition=39	% Inhibition=78	% Inhibition=76	% Inhibition=81
			
% Inhibition=78	% Inhibition=83	% Inhibition=80	% Inhibition=84
			
% Inhibition=79	% Inhibition=72	% Inhibition=58	% Inhibition=71

Section J: Examples L-145 to L-160

			
% inhibition=77	% inhibition=69	% inhibition=66	% inhibition=62
			
% inhibition=70	% inhibition=61	% inhibition=68	% inhibition=53
			
% inhibition=66	% inhibition=77	% inhibition=64	% inhibition=73
			
% inhibition=77	% inhibition=63	% inhibition=78	% inhibition=69

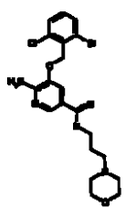
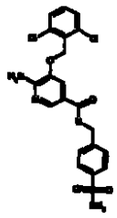
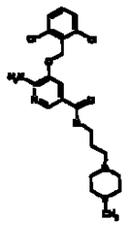
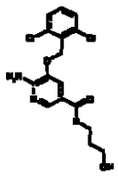
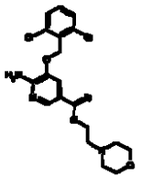
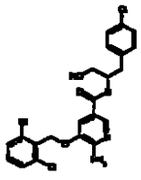
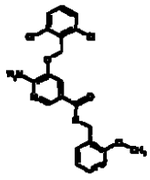
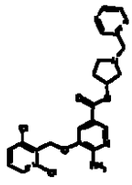
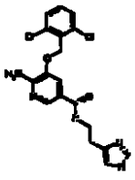
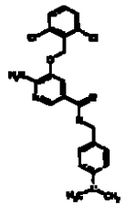
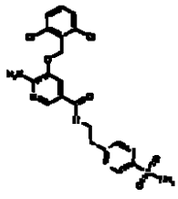
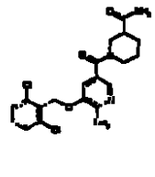
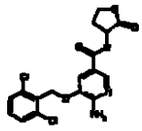
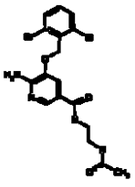
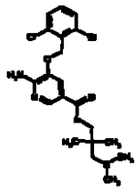
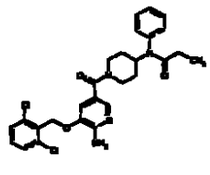
Section K: Examples L-161 to L-176

			
% Inhibition=78	% Inhibition=66	% Inhibition=63	% Inhibition=61
			
% Inhibition=69	% Inhibition=67	% Inhibition=65	% Inhibition=60
			
% Inhibition=78	% Inhibition=77	% Inhibition=69	% Inhibition=79
			
% Inhibition=63	% Inhibition=66	% Inhibition=60	% Inhibition=61

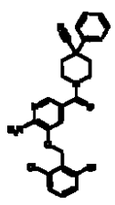
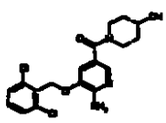
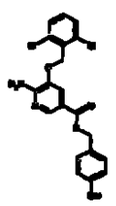
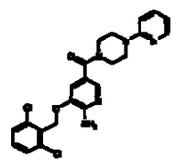
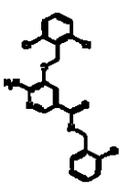
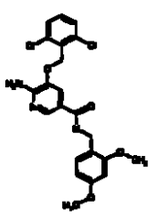
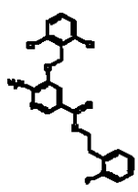
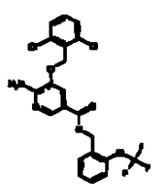
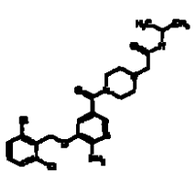
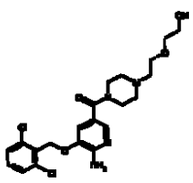
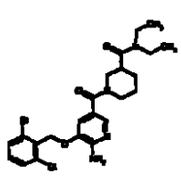
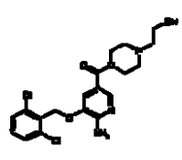
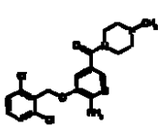
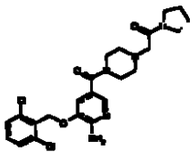
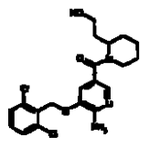
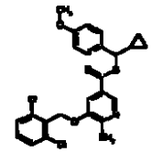
136

Table 6

Section A: Examples L-177 to L-192

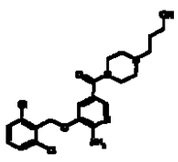
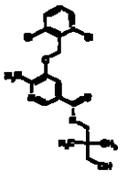
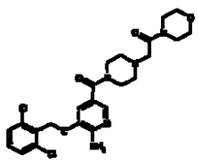
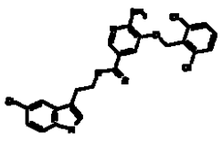
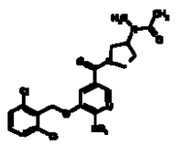
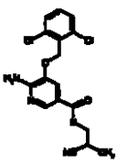
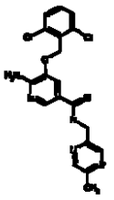
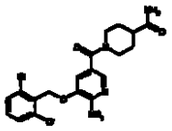
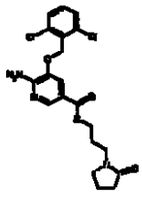
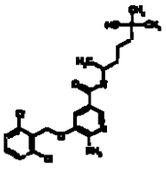
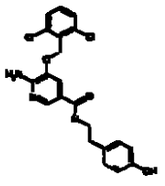
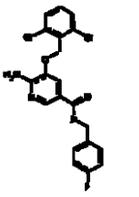
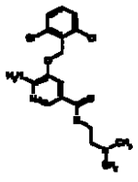
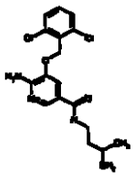
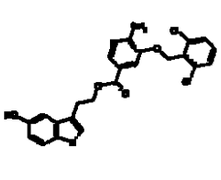
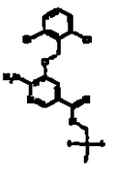
			
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Section B: Examples L-193 to L-208

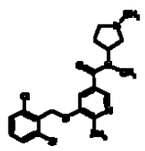
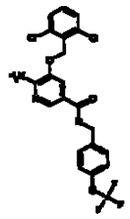
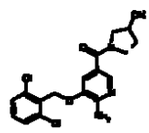
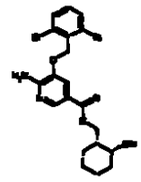
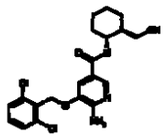
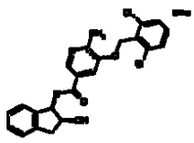
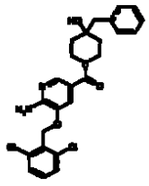
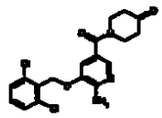
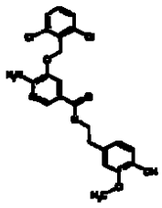
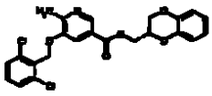
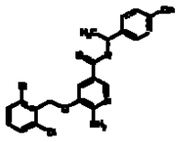
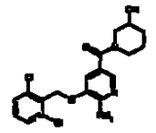
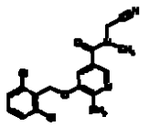
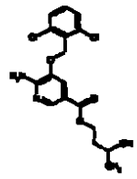
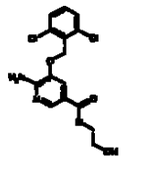
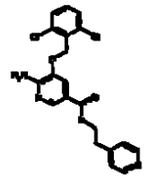
			
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137

Section C: Examples L-209 to L-224

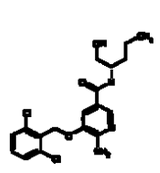
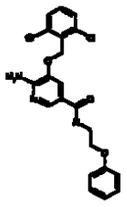
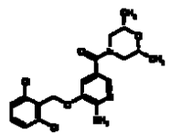
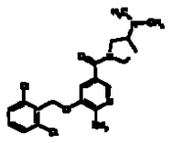
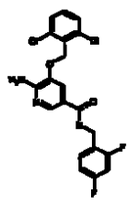
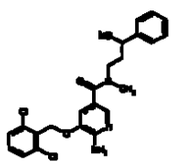
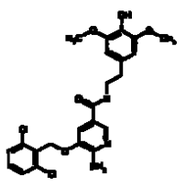
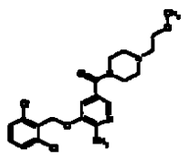
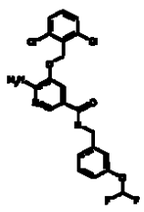
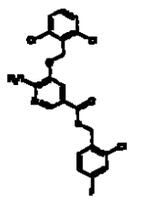
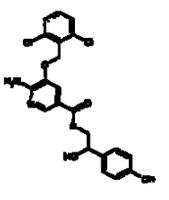
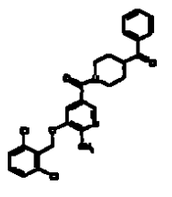
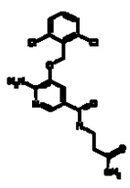
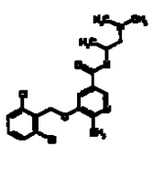
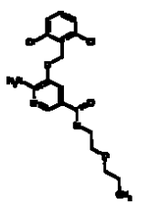
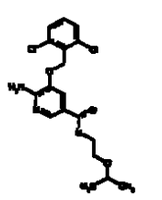
			
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Section D: Examples L-225 to L-240

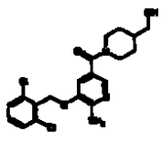
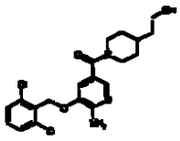
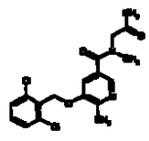
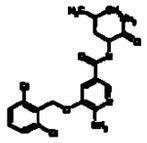
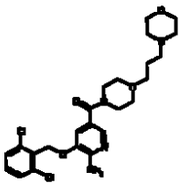
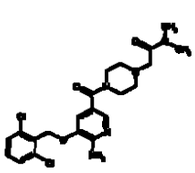
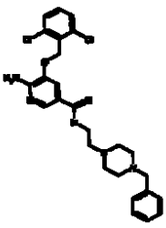
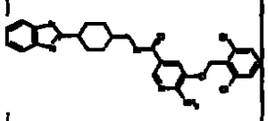
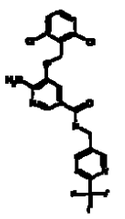
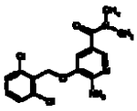
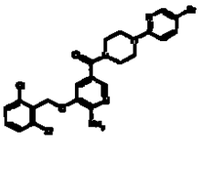
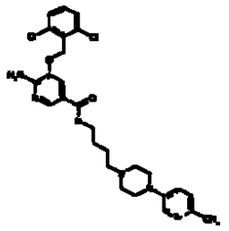
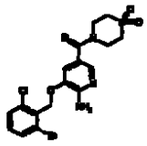
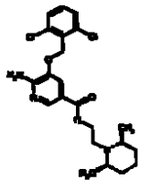
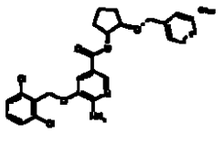
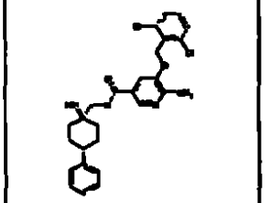
			
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% Inhibition=24	% Inhibition=23	% Inhibition=82	% Inhibition=14
			
% Inhibition=32	% Inhibition=24	% Inhibition=38	% Inhibition=33
			
% Inhibition=30	% Inhibition=35	% Inhibition=34.	% Inhibition=30

B8

Section E: Examples L-241 to L-256

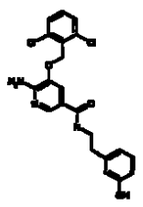
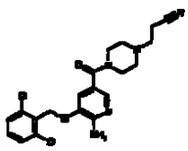
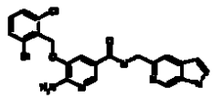
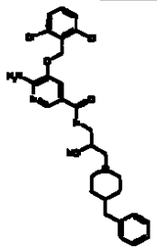
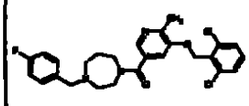
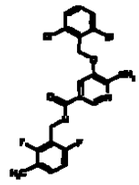
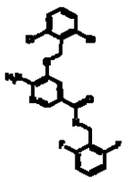
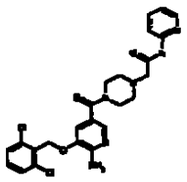
			
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% Inhibition=33	% Inhibition=28	% Inhibition=25	% Inhibition=27
			
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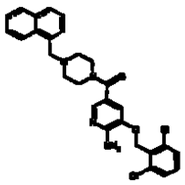
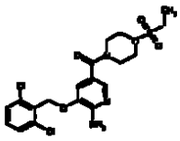
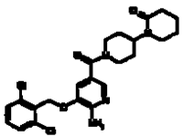
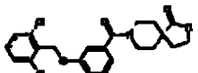
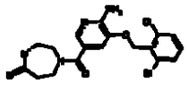
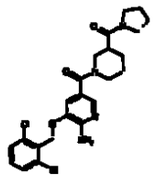
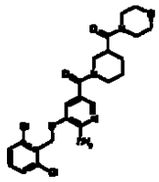
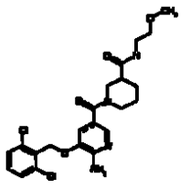
Section F: Examples L-257 to L-272

			
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% Inhibition=10	% Inhibition=-2	% Inhibition=16	% Inhibition=15

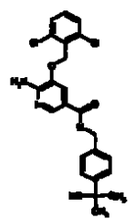
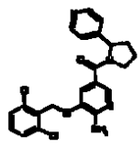
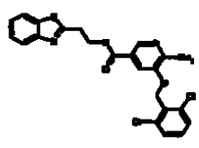
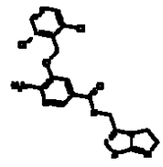
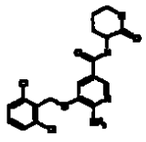
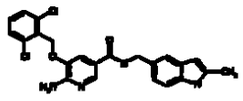
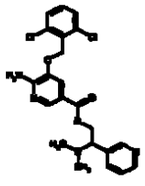
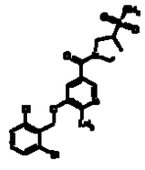
131

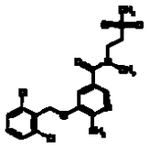
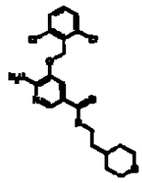
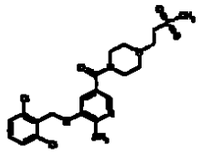
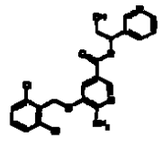
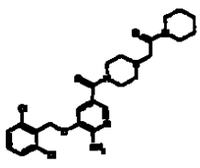
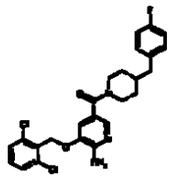
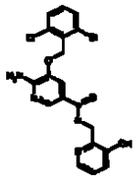
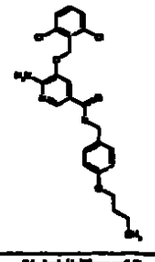
Section G: Examples L-273 to L-288

			
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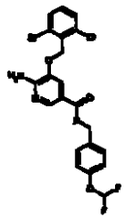
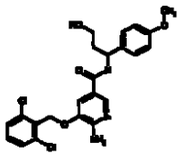
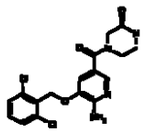
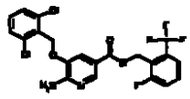
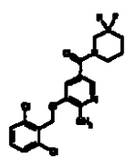
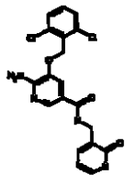
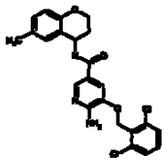
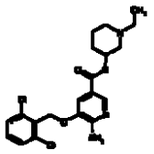
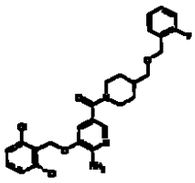
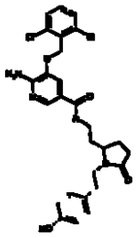
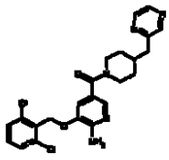
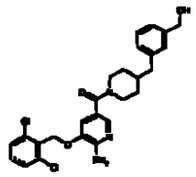
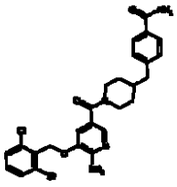
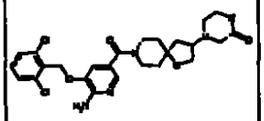
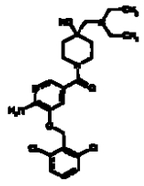
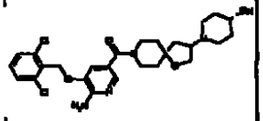
			
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% Inhibition=31	% Inhibition=47	% Inhibition=21	% Inhibition=20

Section G: Examples L-289 to L-304

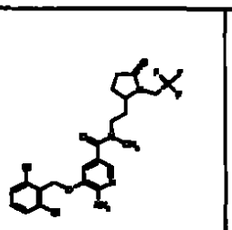
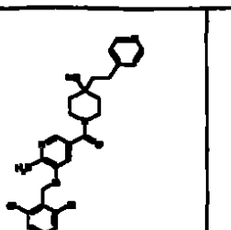
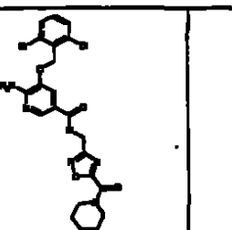
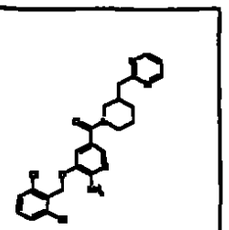
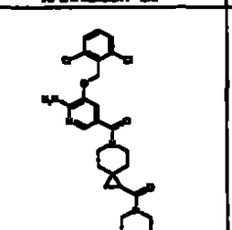
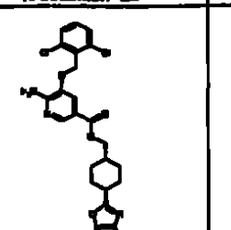
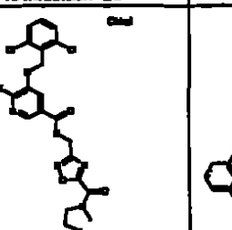
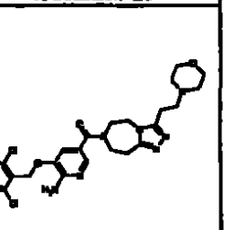
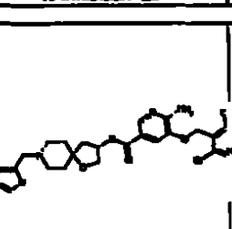
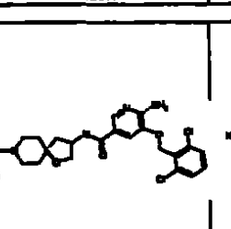
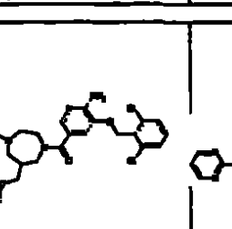
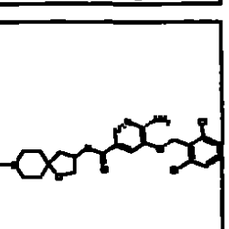
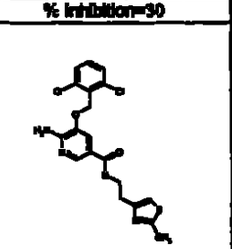
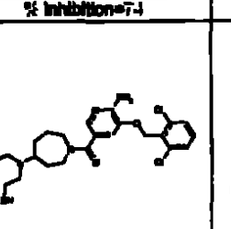
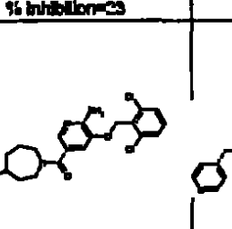
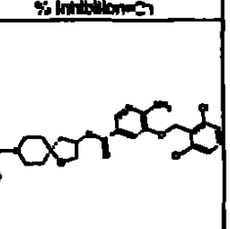
			
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Section I: Examples L-305 to L-320

			
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Section J: Examples L-321 to L-336

			
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Section K: Examples L-337 to L-352

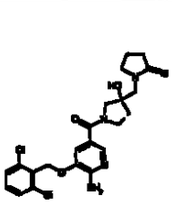
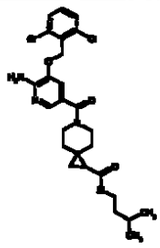
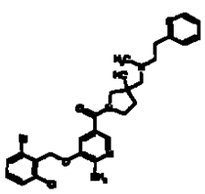
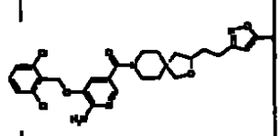
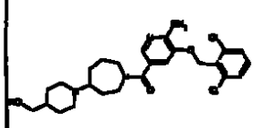
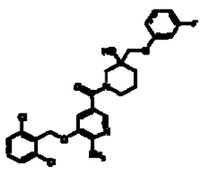
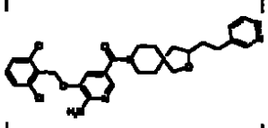
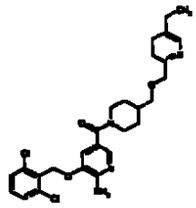
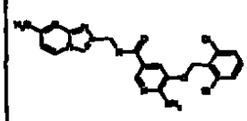
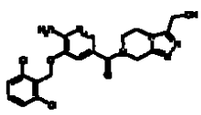
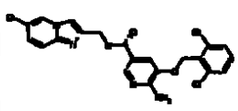
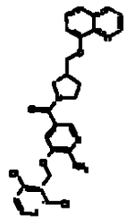
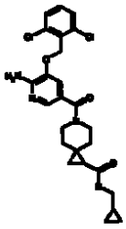
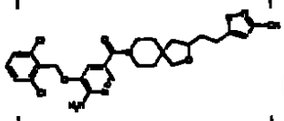
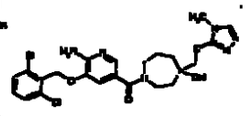
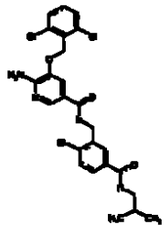
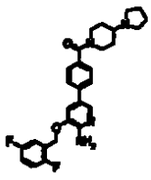
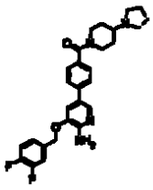
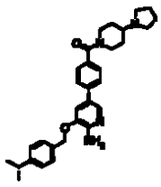
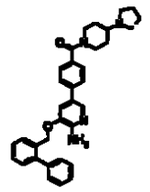
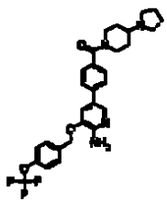
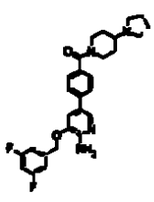
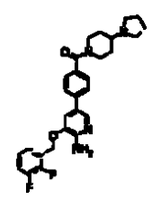
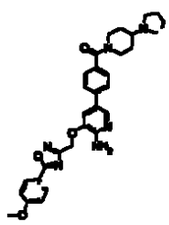
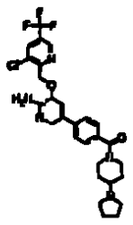
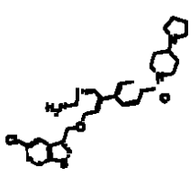
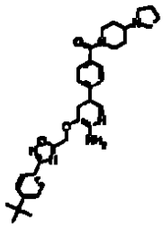
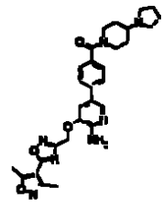
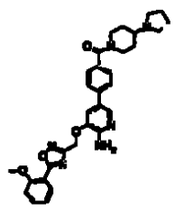
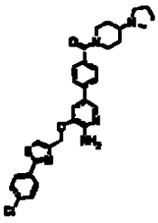
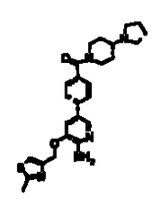
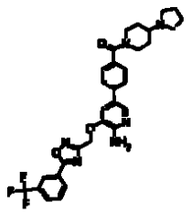
			
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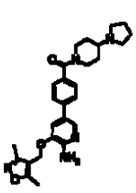
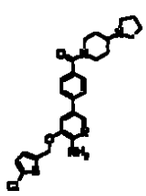
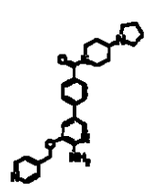
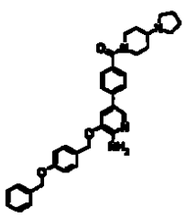
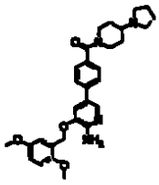
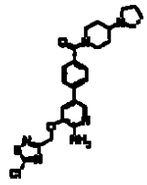
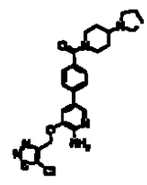
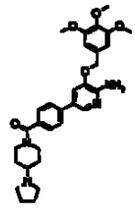
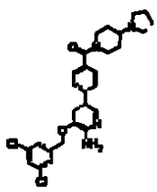
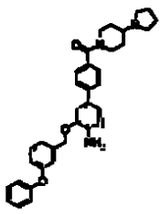
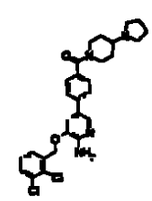
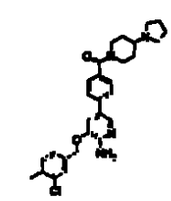
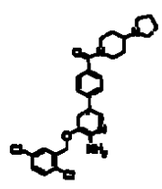
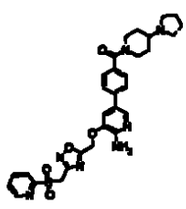
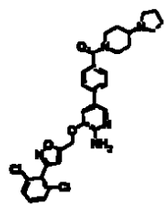
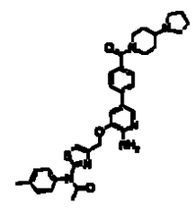
Table 7

Section A: Examples L-353 to L-368

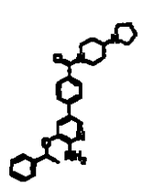
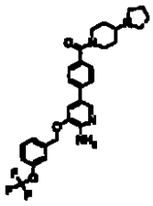
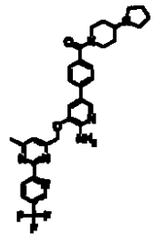
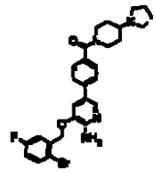
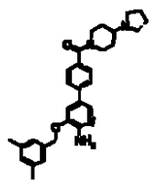
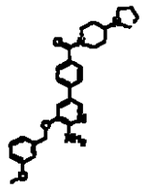
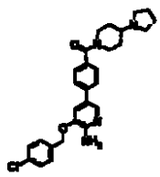
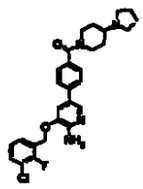
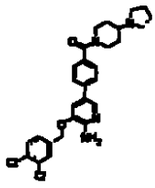
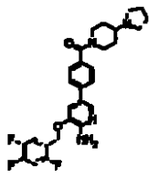
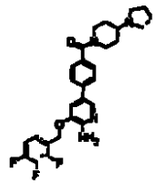
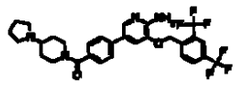
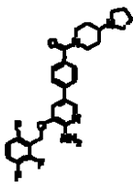
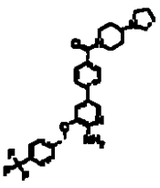
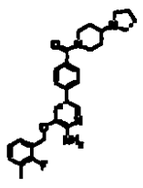
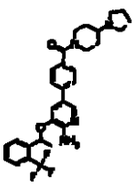
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142

Section B: Examples L-369 to L-384

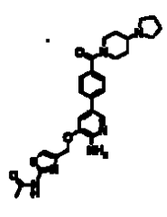
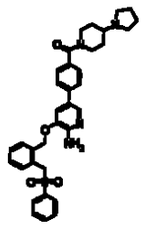
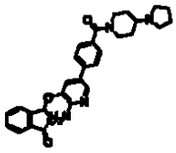
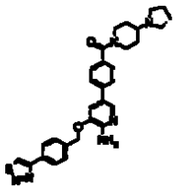
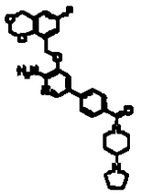
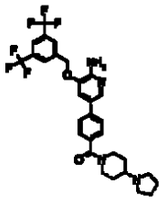
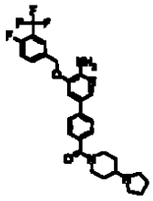
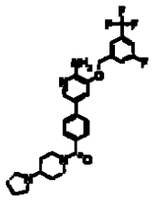
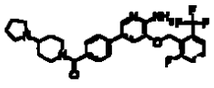
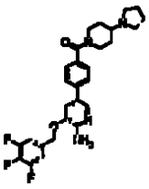
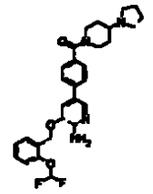
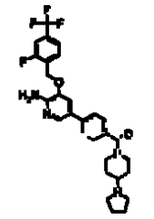
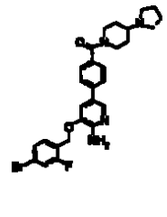
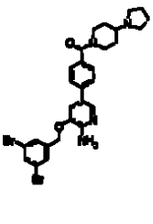
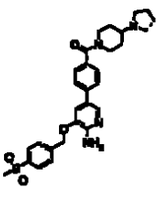
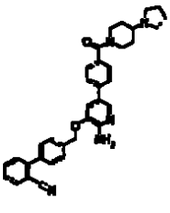
			
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Section C: Examples L-385 to L-400

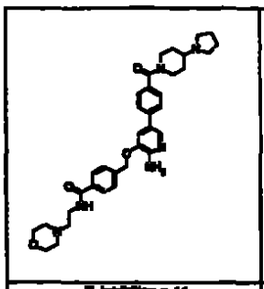
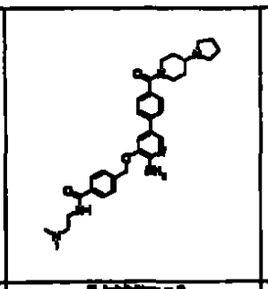
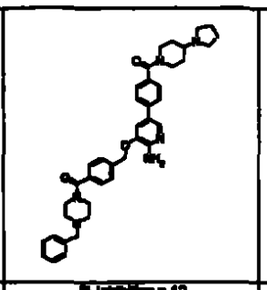
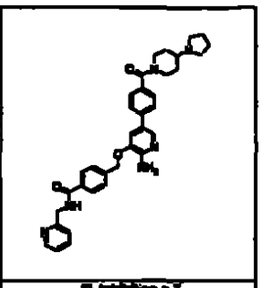
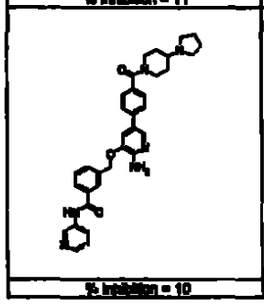
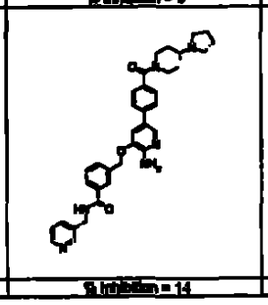
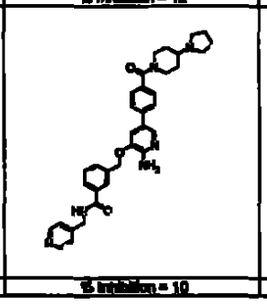
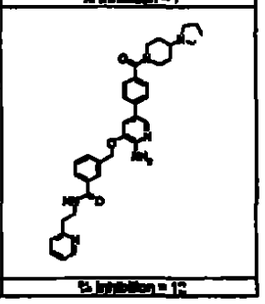
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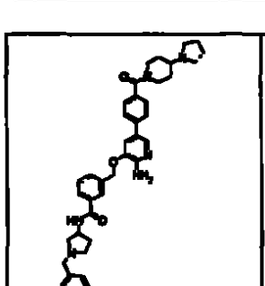
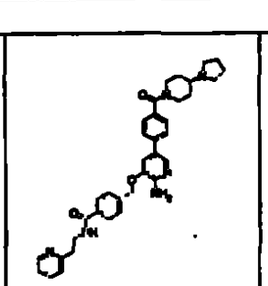
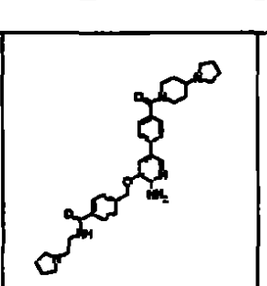
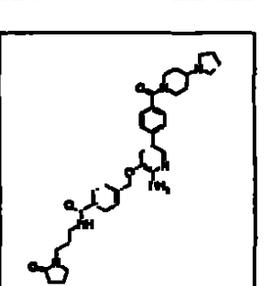
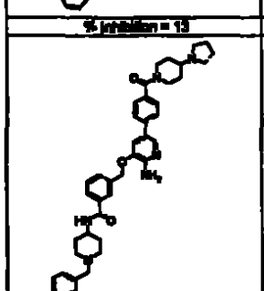
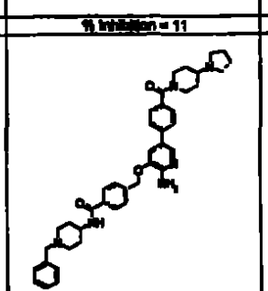
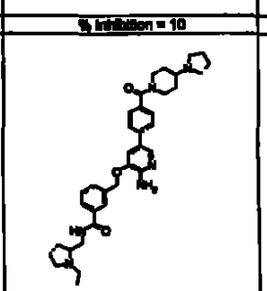
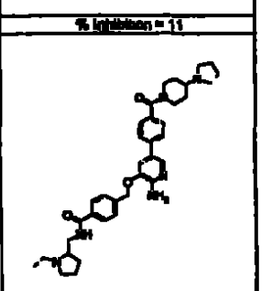
123

Section D: Examples L-401 to L-416

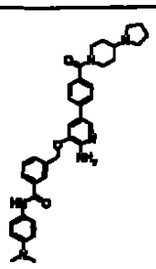
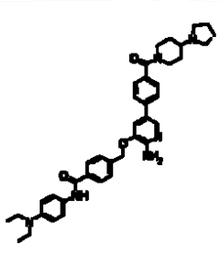
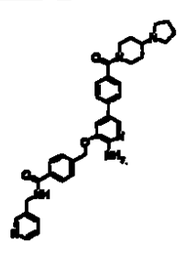
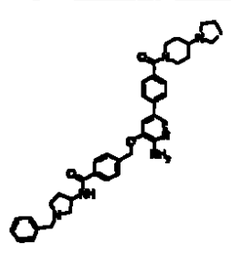
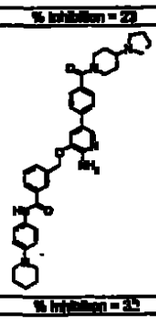
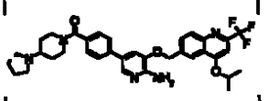
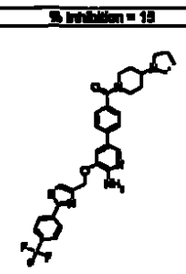
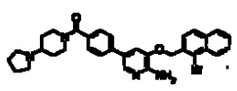
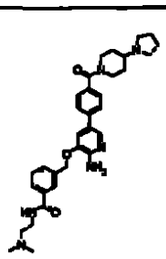
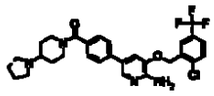
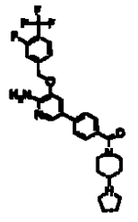
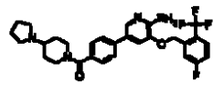
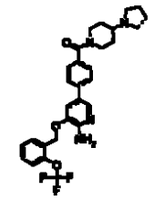
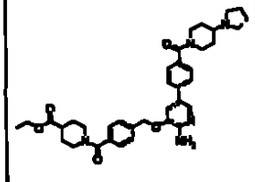
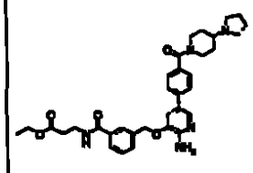
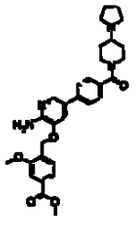
			
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Section E: Examples L-417 to L-432

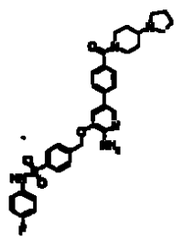
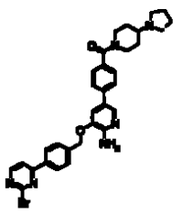
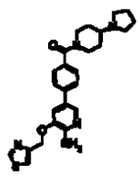
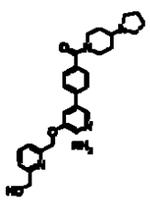
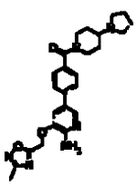
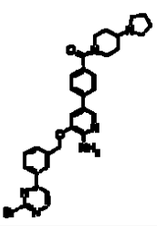
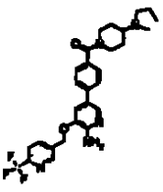
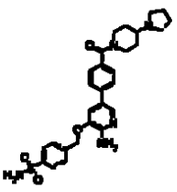
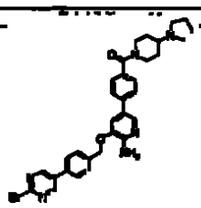
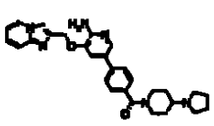
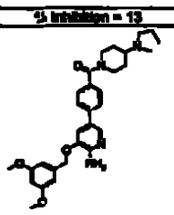
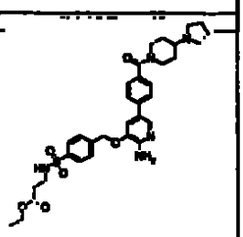
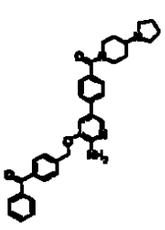
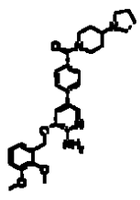
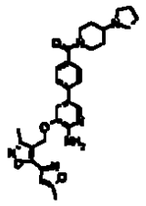
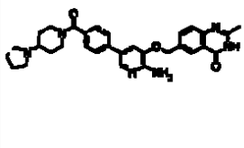
			
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% Inhibition = 10	% Inhibition = 14	% Inhibition = 10	% Inhibition = 12

			
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% Inhibition = 13	% Inhibition = 11	% Inhibition = 10	% Inhibition = 18

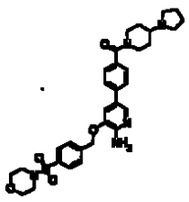
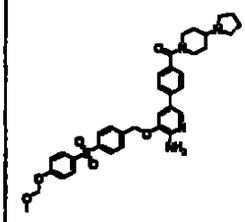
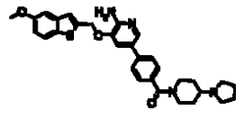
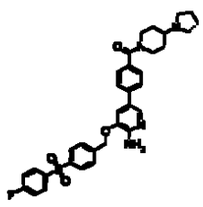
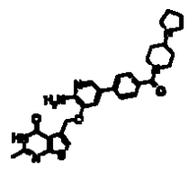
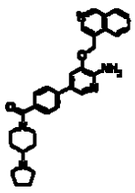
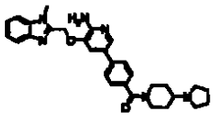
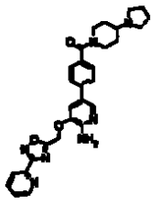
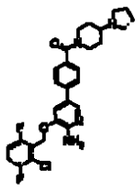
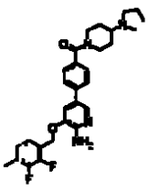
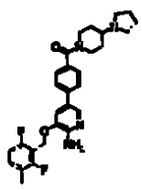
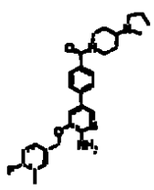
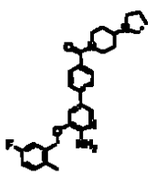
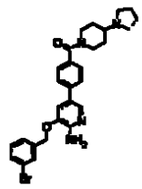
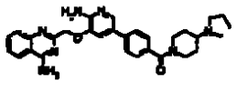
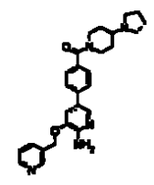
Section F: Examples L-433 to L-448

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 % Inhibition = 35	 % Inhibition = 19	 % Inhibition = 21	 % Inhibition = 89
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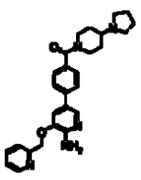
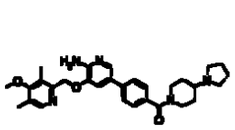
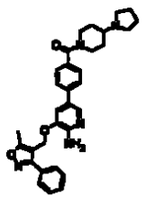
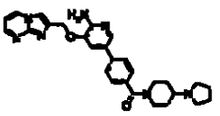
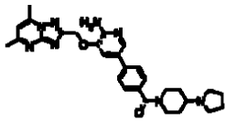
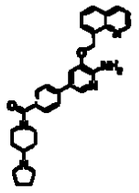
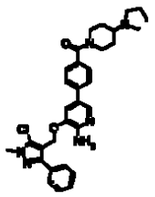
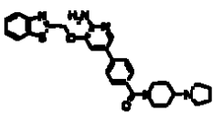
Section G: Examples L-449 to L-464

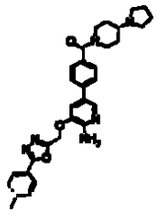
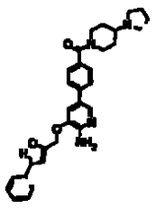
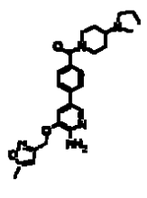
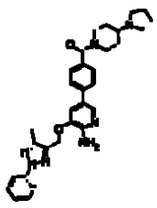
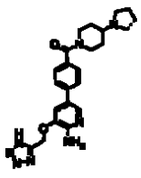
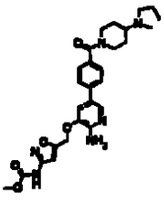
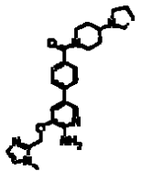
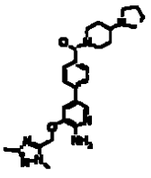
			
% Inhibition = 15	% Inhibition = 17	% Inhibition = 12	% Inhibition = 16
			
	% Inhibition = 13	% Inhibition = 13	
			
% Inhibition = 31	% Inhibition = 11	% Inhibition = 17	% Inhibition = 15
			
% Inhibition = 21	% Inhibition = 23	% Inhibition = 22	% Inhibition = 12

Section H: Examples L-465 to L-480

			
% Inhibition = 14	% Inhibition = 18	% Inhibition = 13	% Inhibition = 13
			
% Inhibition = 19	% Inhibition = 9	% Inhibition = 10	% Inhibition = 9
			
% Inhibition = 80	% Inhibition = 39	% Inhibition = 51	% Inhibition = 37
			
% Inhibition = 29	% Inhibition = 34	% Inhibition = 16	% Inhibition = 17

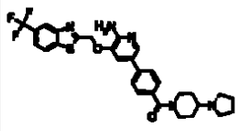
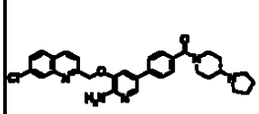
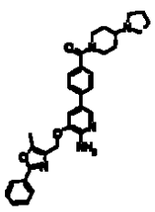
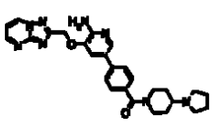
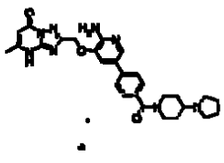
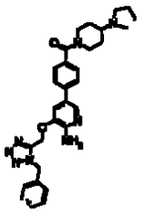
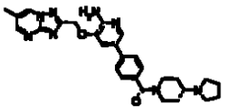
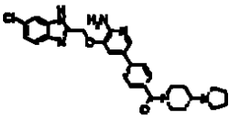
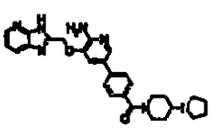
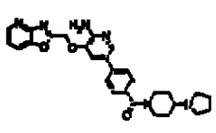
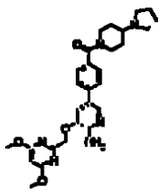
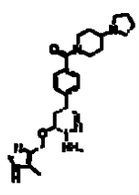
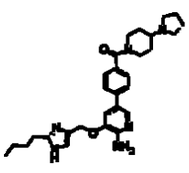
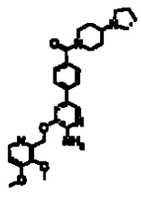
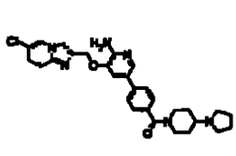
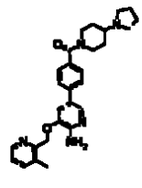
Section I: Examples L-481 to L-496

			
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% Inhibition = 18	% Inhibition = 22	% Inhibition = 63	% Inhibition = 17

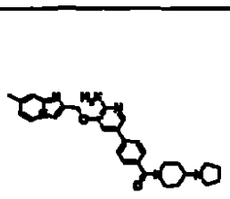
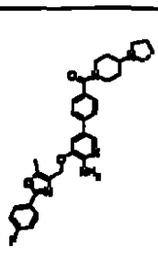
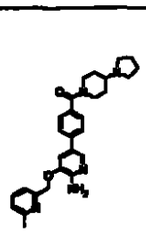
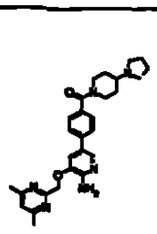
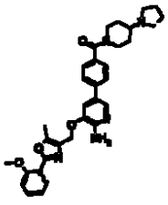
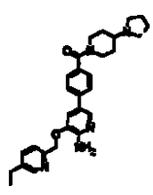
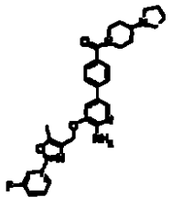
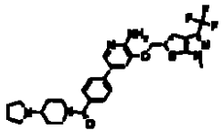
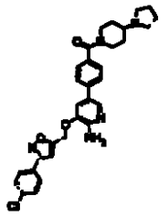
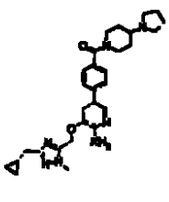
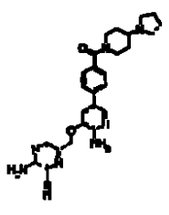
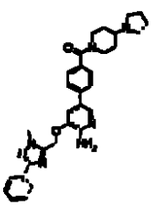
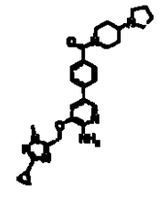
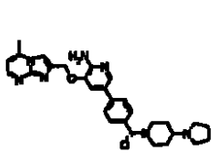
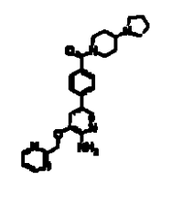
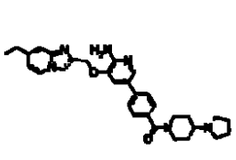
			
% Inhibition = 18	% Inhibition = 23	% Inhibition = 18	% Inhibition = 22
			
% Inhibition = 14	% Inhibition = 18	% Inhibition = 14	% Inhibition = 14

146

Section J: Examples L-497 to L-512

			
% Inhibition = 34	% Inhibition = 24	% Inhibition = 18	% Inhibition = 19
			
% Inhibition = 18	% Inhibition = 19	% Inhibition = 17	% Inhibition = 18
			
% Inhibition = 17	% Inhibition = 17	% Inhibition = 20	% Inhibition = 12
			
% Inhibition = 18	% Inhibition = 23	% Inhibition = 18	% Inhibition = 18

Section K: Examples L-513 to L-528

			
% Inhibition = 16	% Inhibition = 17	% Inhibition = 17	% Inhibition = 16
			
% Inhibition = 16	% Inhibition = 15	% Inhibition = 8	% Inhibition = 14
			
% Inhibition = 23	% Inhibition = 7	% Inhibition = 6	% Inhibition = 8
			
% Inhibition = 5	% Inhibition = 10	% Inhibition = 9	% Inhibition = 9

147

Section L: Examples L-529 to L-548

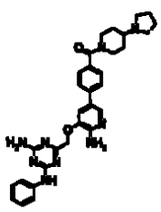
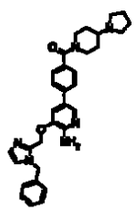
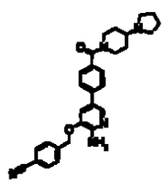
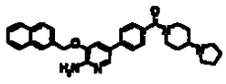
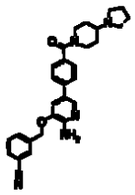
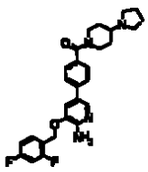
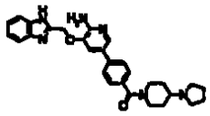
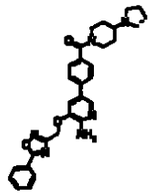
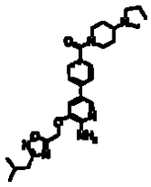
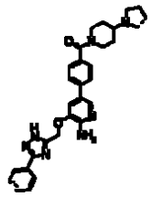
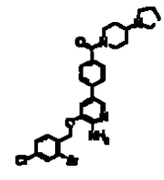
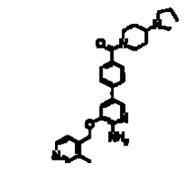
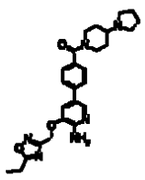
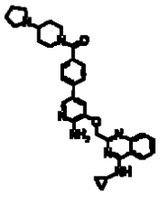
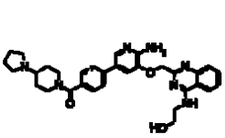
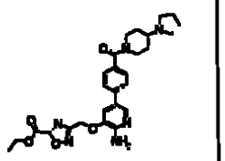
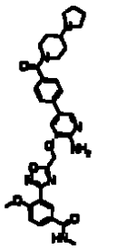
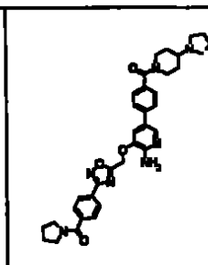
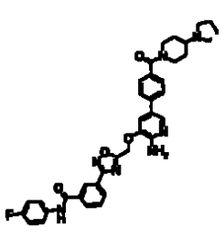
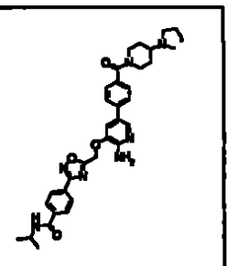
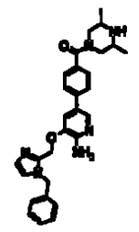
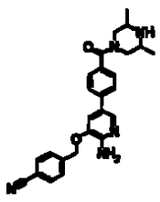
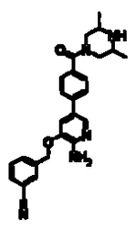
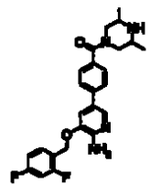
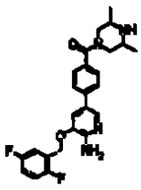
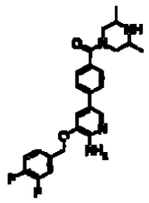
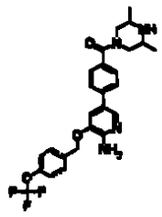
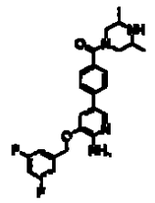
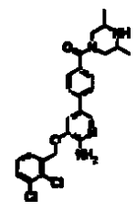
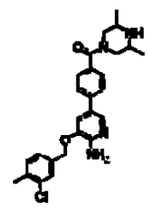
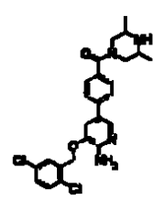
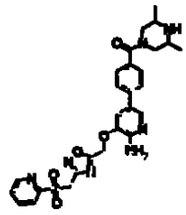
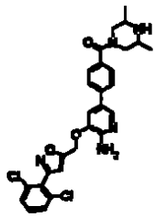
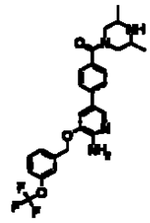
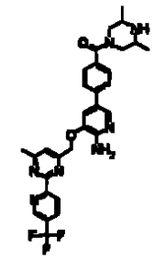
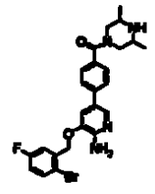
			
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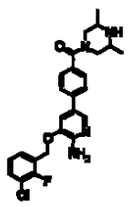
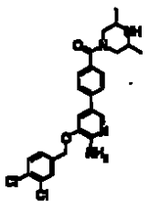
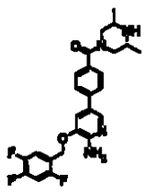
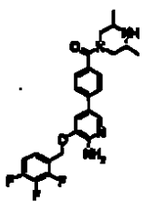
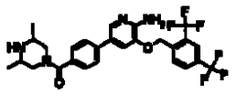
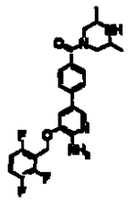
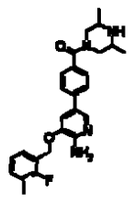
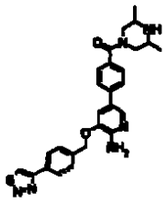
Table 8

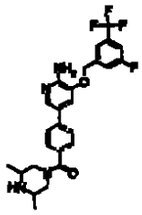
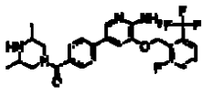
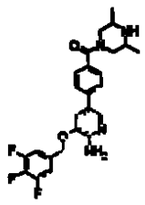
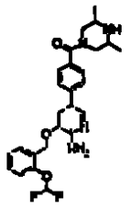
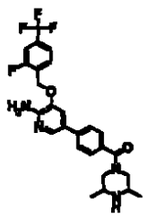
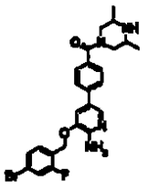
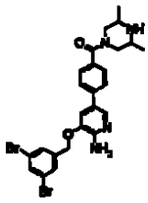
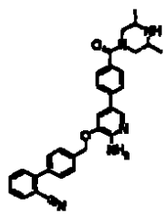
Section A: Examples L-549 to L-561

			
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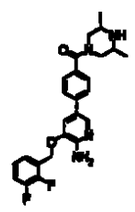
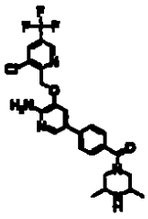
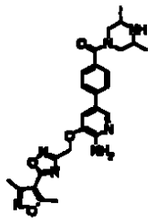
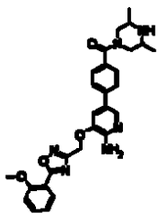
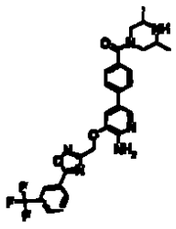
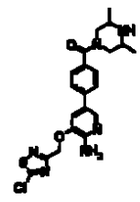
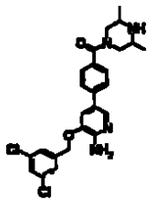
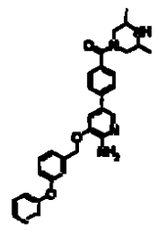
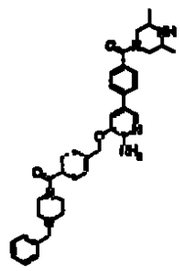
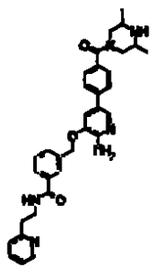
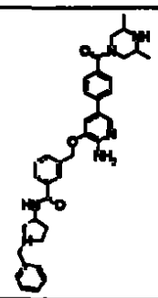
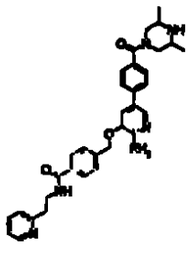
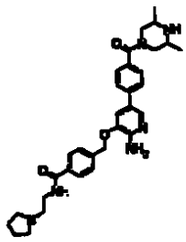
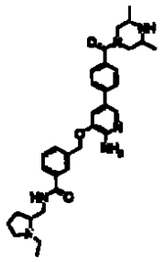
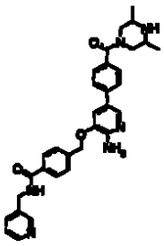
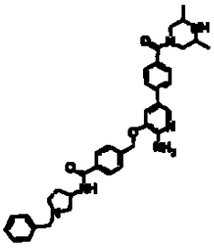
148

Section B: Examples L-565 to L-580

			
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% Inhibition = 22	% Inhibition = 41	% Inhibition = 28	% Inhibition = 17

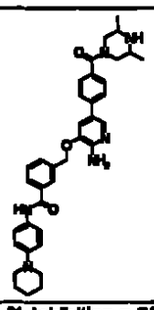
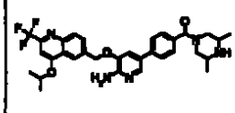
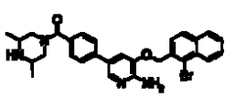
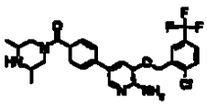
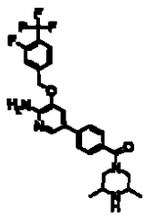
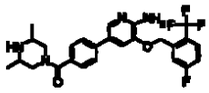
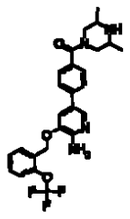
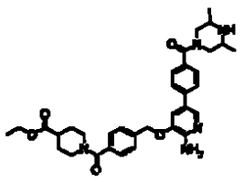
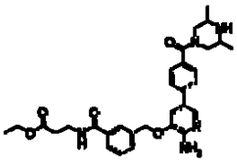
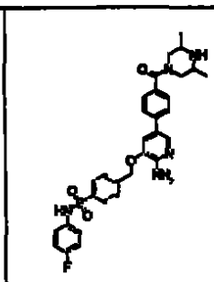
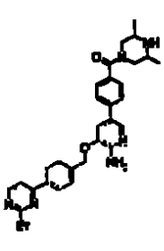
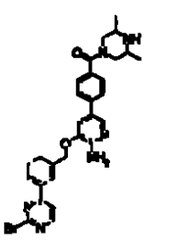
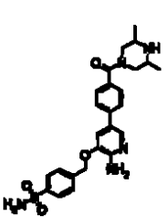
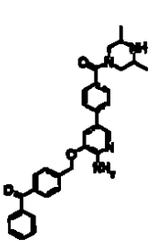
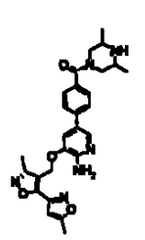
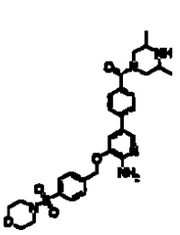
			
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% Inhibition = 24	% Inhibition = 29	% Inhibition = 42	% Inhibition = 73

Section C: Examples L-581 to L-596

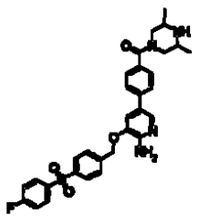
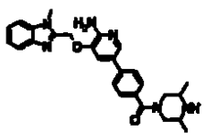
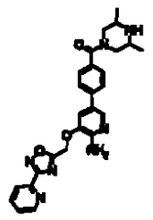
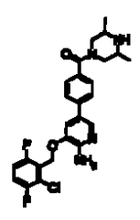
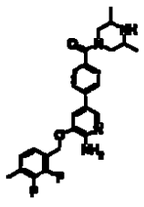
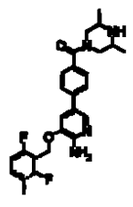
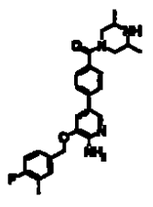
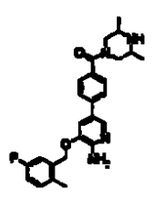
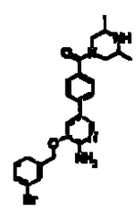
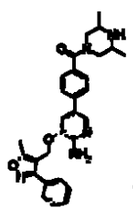
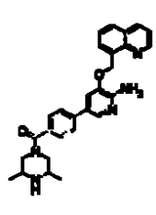
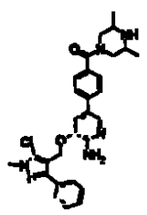
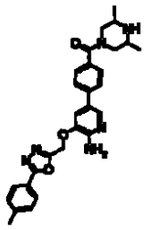
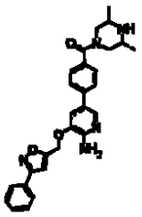
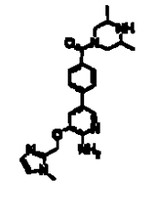
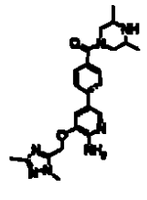
			
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% Inhibition = 30	% Inhibition = 6	% Inhibition = 28	% Inhibition = 32
			
% Inhibition = 15	% Inhibition = 18	% Inhibition = 18	% Inhibition = 19
			
% Inhibition = 12	% Inhibition = 10	% Inhibition = 8	% Inhibition = 19

129

Section D: Examples L-597 to L-612

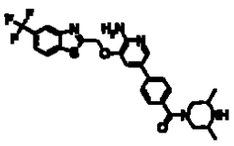
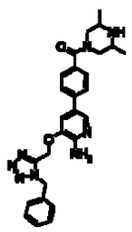
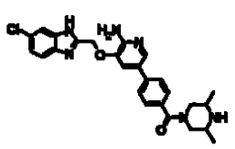
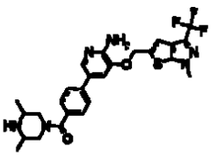
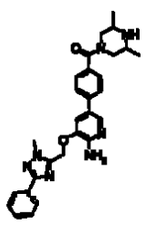
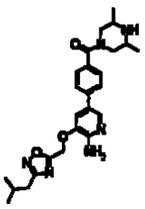
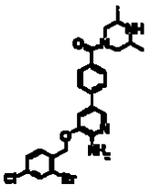
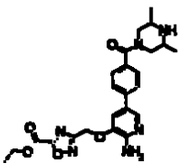
			
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% Inhibition = 17	% Inhibition = 17	% Inhibition = 20	% Inhibition = 12
			
% Inhibition = 14	% Inhibition = 14	% Inhibition = 17	% Inhibition = 19
			
% Inhibition = 18	% Inhibition = 35	% Inhibition = 25	% Inhibition = 13

Section E: Examples L-613 to L-628

			
% Inhibition = 13	% Inhibition = 16	% Inhibition = 15	% Inhibition = 51
			
% Inhibition = 37	% Inhibition = 35	% Inhibition = 16	% Inhibition = 28
			
% Inhibition = 21	% Inhibition = 16	% Inhibition = 17	% Inhibition = 16
			
% Inhibition = 14	% Inhibition = 16	% Inhibition = 12	% Inhibition = 13

150

Section F: Examples L-629 to L-636

			
% Inhibition = 27	% Inhibition = 15	% Inhibition = 10	% Inhibition = 13
			
% Inhibition = 13	% Inhibition = 14	% Inhibition = 29	% Inhibition = 13

PAG 240.

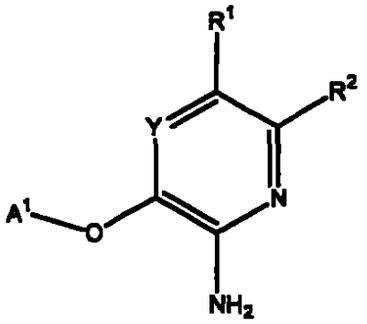
The present invention is not to be limited in scope by the exemplified aspects which are intended as illustrations of single aspects of the invention, and any clones, DNA or amino acid sequences which are functionally equivalent are within the scope of the invention. Indeed, various modifications of the invention in addition to those described herein will become apparent to those skilled in the art from the foregoing description and accompanying drawings. Such modifications are intended to fall within the scope of the appended claims.

The disclosure of U.S. Provisional Application Serial No. 60/449,588, filed February 26, 2003, and U.S. Provisional Application Serial No. 60/540,229, filed January 29, 2004, are hereby incorporated by reference in their entireties.

All references cited herein are hereby incorporated by reference in their entireties.

We Claim:

1. A compound of formula 1



1

wherein:

Y is N or CR^{12};

R^1 is selected from C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl, 3-12 membered heteroalicyclic, $-O(CR^6R^7)_nR^4$, $-C(O)R^4$, $-C(O)OR^4$, -CN, $-NO_2$, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-C(O)NR^4R^5$, $-NR^4C(O)R^5$, $-C(=NR^5)NR^4R^5$, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl; and each hydrogen in R^1 is optionally substituted by one or more R^3 groups;

R^2 is hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-O(CR^6R^7)_nR^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-C(=NR^6)NR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$, and each hydrogen in R^2 is optionally substituted by one or more R^8 groups;

R^3 is halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-O(CR^6R^7)_nR^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-C(=NR^6)NR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$, each hydrogen in R^3 is optionally substituted by one or more R^8 groups, and R^3 groups on adjacent atoms may combine to form a C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heteroalicyclic group;

each R^4, R^5, R^6 and R^7 is independently hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl; or any two of R^4, R^5, R^6 and R^7 bound to the same nitrogen atom may, together with the nitrogen to which they are bound, be combined to form a 3 to 12 membered heteroalicyclic or 5-12 membered heteroaryl group optionally containing 1 to 3 additional heteroatoms selected from N, O, and S; or any two of R^4, R^5, R^6 and R^7 bound to the same carbon atom may be combined to form a C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic or 5-12 membered heteroaryl group; and each hydrogen in R^4, R^5, R^6 and R^7 is optionally substituted by one or more R^8 groups;

each R^8 is independently halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, -CN, $-O-C_{1-12}$ alkyl, $-O-(CH_2)_nC_{3-12}$ cycloalkyl, $-O-(CH_2)_nC_{6-12}$ aryl, $-O-(CH_2)_n$(3-12 membered heteroalicyclic) or $-O-(CH_2)_n$(5-12 membered heteroaryl); and each hydrogen in R^8 is optionally substituted by one or more R^{11} groups;

A^1 is $-(CR^9R^{10})_n-A^2$ except that:

(i) when Y is N and R^1 is substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl, A^1 is $-(CR^9R^{10})_n-A^2$ and *n* is not zero; and

(ii) when Y is N and R^2 is H and A^1 is m-chlorobenzyl, R^1 is not unsubstituted piperazine;

each R^9 and R^{10} is independently hydrogen, halogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, $-CN$, $-C(O)R^4$, $-OC(O)R^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$; R^9 and R^{10} may combine to form a C_{3-12} cycloalkyl, 3-12 membered heterocalicyclic, C_{6-12} aryl or 5-12 membered heteroaryl ring; and each hydrogen in R^9 and R^{10} is optionally substituted by one or more R^3 groups;

A^2 is C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heterocalicyclic, and A^2 is optionally substituted by one or more R^3 groups;

each R^{11} is independently halogen, C_{1-12} alkyl, C_{1-12} alkoxy, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, $-O-C_{1-12}$ alkyl, $-O-(CH_2)_nC_{3-12}$ cycloalkyl, $-O-(CH_2)_nC_{6-12}$ aryl, $-O-(CH_2)_n$(3-12 membered heterocalicyclic), $-O-(CH_2)_n$(5-12 membered heteroaryl) or $-CN$, and each hydrogen in R^{11} is optionally substituted by one or more groups selected from halogen, $-OH$, $-CN$, $-C_{1-12}$ alkyl which may be partially or fully halogenated, $-O-C_{1-12}$ alkyl which may be partially or fully halogenated, $-CO$, $-SO$ and $-SO_2$;

R^{12} is hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, $-CN$, $-C(O)R^4$, $-OC(O)R^4$, $-O(CR^6R^7)_nR^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-C(=NR^5)NR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$, and each hydrogen in R^{12} is optionally substituted by one or more R^3 groups;

R^1 and R^2 or R^1 and R^{12} may be combined together to form a C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heterocalicyclic group;

m is 0, 1 or 2;

n is 0, 1, 2, 3 or 4; and

p is 1 or 2;

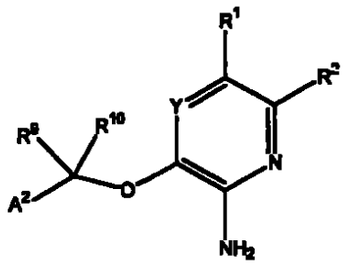
or a pharmaceutically acceptable salt, solvate or hydrate thereof.

2. The compound of claim 1, wherein Y is N.

3. The compound of claim 1, wherein Y is CR^{12}.

4. The compound of claim 1, wherein the compound has formula 1a

152



1a

wherein A^2 is C_{6-12} aryl or 5-12 membered heteroaryl optionally substituted by one or more R^3 groups.

5. The compound of claim 4, wherein R^1 is selected from C_{6-12} aryl and 5-12 membered heteroaryl, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

6. The compound of claim 4, wherein R^1 is selected from C_{3-12} cycloalkyl, 3-12 membered heterocalicyclic, $-O(CR^6R^7)_nR^4$, $-C(O)R^4$, $-C(O)OR^4$, $-CN$, $-NO_2$, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-C(O)NR^4R^5$, $-NR^4C(O)R^5$, $-C(=NR^5)NR^4R^5$, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl; and each hydrogen in R^1 is optionally substituted by one or more R^2 groups.

7. The compound of claim 4, wherein A^2 is substituted by at least one halogen atom.

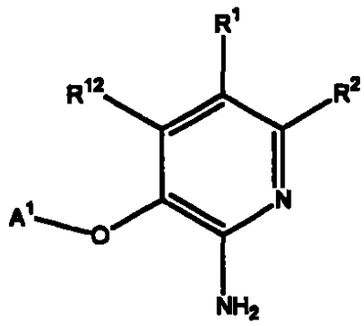
8. The compound of claim 4, wherein R^2 is hydrogen, R^9 and R^{10} are independently C_{1-4} alkyl, and A^2 is phenyl substituted by at least one halogen atom.

9. The compound of claim 1, wherein R^1 is a furan, thiopene, pyrrole, pyrroline, pyrrolidine, dioxolane, oxazole, thiazole, imidazole, imidazoline, imidazolidine, pyrazole, pyrazoline, pyrazolidine, isoxazole, isothiazole, oxadiazole, triazole, thiadiazole, pyran, pyridine, piperidine, dioxane, morpholine, dithiane, thiomorpholine, pyridazine, pyrimidine, pyrazine, piperazine, triazine, trithiane or phenyl group, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

10. The compound of claim 1, wherein R^1 is a fused ring heteroaryl group, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

11. The compound of claim 1, wherein R^1 is a $-SO_2NR^4R^5$ group.

12. A compound of formula 2



2

wherein:

R^1 is selected from C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl, 3-12 membered heteroalicyclic, $-O(CR^6R^7)_mR^4$, $-C(O)R^4$, $-C(O)OR^4$, -CN, $-NO_2$, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-C(O)NR^4R^5$, $-NR^4C(O)R^5$, $-C(=NR^6)NR^4R^5$, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl; and each hydrogen in R^1 is optionally substituted by one or more R^3 groups;

R^2 is hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-O(CR^6R^7)_mR^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-C(=NR^6)NR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$, and each hydrogen in R^2 is optionally substituted by one or more R^8 groups;

R^3 is halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-O(CR^6R^7)_mR^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-C(=NR^6)NR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$, each hydrogen in R^3 is optionally substituted by one or more R^8 groups, and R^3 groups on adjacent atoms may combine to form a C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heteroalicyclic group;

each R^4, R^5, R^6 and R^7 is independently hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl; or any two of R^4, R^5, R^6 and R^7 bound to the same nitrogen atom may, together with the nitrogen to which they are bound, be combined to form a 3 to 12 membered heteroalicyclic or 5-12 membered heteroaryl group optionally containing 1 to 3 additional heteroatoms selected from N, O, and S; or any two of R^4, R^5, R^6 and R^7 bound to the same carbon atom may be combined to form a C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic or 5-12 membered heteroaryl group; and each hydrogen in R^4, R^5, R^6 and R^7 is optionally substituted by one or more R^8 groups;

each R^8 is independently halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, -CN, $-O-C_{1-12}$ alkyl, $-O-(CH_2)_nC_{3-12}$ cycloalkyl, $-O-(CH_2)_nC_{6-12}$ aryl, $-O-(CH_2)_n$(3-12 membered heteroalicyclic) or $-O-(CH_2)_n$(5-12 membered heteroaryl); and each hydrogen in R^8 is optionally substituted by one or more R^{11} groups;

A^1 is $-(CR^9R^{10})_n-A^2$;

each R^9 and R^{10} is independently hydrogen, halogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$,

153

$-(CR^8R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-NR^4C(O)R^5$, $-(CR^8R^7)_nC(O)OR^4$, $-(CR^8R^7)_nNCR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$; R^9 and R^{10} may combine to form a C_{3-12} cycloalkyl, 3-12 membered heteroalicyclic, C_{6-12} aryl or 5-12 membered heteroaryl ring; and each hydrogen in R^9 and R^{10} is optionally substituted by one or more R^3 groups;

A^2 is C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heteroalicyclic, and A^2 is optionally substituted by one or more R^3 groups;

each R^{11} is independently halogen, C_{1-12} alkyl, C_{1-12} alkoxy, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, $-O-C_{1-12}$ alkyl, $-O-(CH_2)_nC_{3-12}$ cycloalkyl, $-O-(CH_2)_nC_{6-12}$ aryl, $-O-(CH_2)_n$(3-12 membered heteroalicyclic), $-O-(CH_2)_n$(5-12 membered heteroaryl) or -CN, and each hydrogen in R^{11} is optionally substituted by one or more groups selected from halogen, -OH, -CN, $-C_{1-12}$ alkyl which may be partially or fully halogenated, $-O-C_{1-12}$ alkyl which may be partially or fully halogenated, -CO, -SO and $-SO_2$;

R^{12} is hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^6$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^8R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-O(CR^8R^7)_nR^4$, $-NR^4C(O)R^5$, $-(CR^8R^7)_nC(O)OR^4$, $-(CR^8R^7)_nNCR^4R^5$, $-C(=NR^5)NR^4R^6$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$, and each hydrogen in R^{12} is optionally substituted by one or more R^3 groups;

R^1 and R^2 or R^1 and R^{12} may be combined together to form a C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heteroalicyclic group;

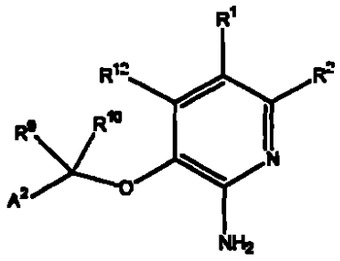
m is 0, 1 or 2;

n is 0, 1, 2, 3 or 4; and

p is 1 or 2;

or a pharmaceutically acceptable salt, solvate or hydrate thereof.

13. The compound of claim 12, wherein the compound has formula 2a



2a

wherein A^2 is C_{6-12} aryl or 5-12 membered heteroaryl optionally substituted by one or more R^3 groups.

14. The compound of claim 13, wherein R^1 is selected from C_{6-12} aryl and 5-12 membered heteroaryl, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

15. The compound of claim 13, wherein R^1 is selected from C_{3-12} cycloalkyl, 3-12 membered heteroalicyclic, $-O(CR^8R^7)_nR^4$, $-C(O)R^4$, $-C(O)OR^4$, -CN, $-NO_2$, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-C(O)NR^4R^5$,

$-NR^4C(O)R^5$, $-C(=NR^5)NR^4R^5$, C_{1-8} alkyl, C_{2-8} alkenyl, and C_{2-8} alkynyl; and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

16. The compound of claim 13, wherein A^2 is substituted by at least one halogen atom.

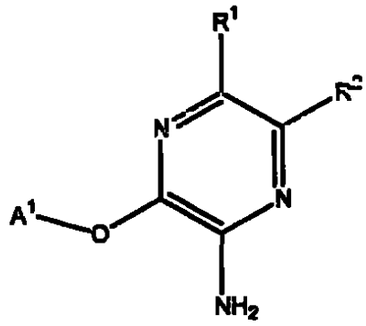
17. The compound of claim 13, wherein R^2 is hydrogen, R^9 and R^{10} are independently C_{1-4} alkyl, and A^2 is phenyl substituted by at least one halogen atom.

18. The compound of claim 12, wherein R^1 is a furan, thiopene, pyrrole, pyrroline, pyrrolidine, dioxolane, oxazole, thiazole, imidazole, imidazoline, imidazolidine, pyrazole, pyrazoline, pyrazolidine, isoxazole, isothiazole, oxadiazole, triazole, thiadiazole, pyran, pyridine, piperidine, dioxane, morpholine, dithiane, thiomorpholine, pyridazine, pyrimidine, pyrazine, piperazine, triazine, trithiane or phenyl group, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

19. The compound of claim 12, wherein R^1 is a fused ring heteroaryl group, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

20. The compound of claim 12, wherein R^1 is a $-SO_2NR^4R^5$ group.

21. A compound of formula 3



3

wherein:

R^1 is selected from C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl, 3-12 membered heterocalicyclic, $-O(CR^6R^7)_nR^4$, $-C(O)R^4$, $-C(O)OR^4$, $-CN$, $-NO_2$, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-C(O)NR^4R^5$, $-NR^4C(O)R^5$, $-C(=NR^5)NR^4R^5$, C_{1-8} alkyl, C_{2-8} alkenyl, and C_{2-8} alkynyl; and each hydrogen in R^1 is optionally substituted by one or more R^3 groups;

R^2 is hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, $-CN$, $-C(O)R^4$, $-OC(O)R^4$, $-O(CR^6R^7)_nR^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-C(=NR^6)NR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$, and each hydrogen in R^2 is optionally substituted by one or more R^8 groups;

154

R^3 is halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-O(CR^6R^7)_nR^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-C(=NR^6)NR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$, each hydrogen in R^3 is optionally substituted by one or more R^8 groups, and R^3 groups on adjacent atoms may combine to form a C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heteroalicyclic group;

each R^4, R^5, R^6 and R^7 is independently hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl; or any two of R^4, R^5, R^6 and R^7 bound to the same nitrogen atom may, together with the nitrogen to which they are bound, be combined to form a 3 to 12 membered heteroalicyclic or 5-12 membered heteroaryl group optionally containing 1 to 3 additional heteroatoms selected from N, O, and S; or any two of R^4, R^5, R^6 and R^7 bound to the same carbon atom may be combined to form a C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic or 5-12 membered heteroaryl group; and each hydrogen in R^4, R^5, R^6 and R^7 is optionally substituted by one or more R^8 groups;

each R^8 is independently halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, -CN, $-O-C_{1-12}$ alkyl, $-O-(CH_2)_nC_{3-12}$ cycloalkyl, $-O-(CH_2)_nC_{6-12}$ aryl, $-O-(CH_2)_n$(3-12 membered heteroalicyclic) or $-O-(CH_2)_n$(5-12 membered heteroaryl); and each hydrogen in R^8 is optionally substituted by one or more R^{11} groups;

A^1 is $-(CR^9R^{10})_n-A^2$ except that:

(i) when R^1 is substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl, A^1 is $-(CR^9R^{10})_n-A^2$ and n is not zero; and

(ii) when R^2 is H and A^1 is m-chlorobenzyl, R^1 is not unsubstituted piperazine;

each R^9 and R^{10} is independently hydrogen, halogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$; R^9 and R^{10} may combine to form a C_{3-12} cycloalkyl, 3-12 membered heteroalicyclic, C_{6-12} aryl or 5-12 membered heteroaryl ring; and each hydrogen in R^9 and R^{10} is optionally substituted by one or more R^3 groups;

A^2 is C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heteroalicyclic, and A^2 is optionally substituted by one or more R^3 groups;

each R^{11} is independently halogen, C_{1-12} alkyl, C_{1-12} alkoxy, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, $-O-C_{1-12}$ alkyl, $-O-(CH_2)_nC_{3-12}$ cycloalkyl, $-O-(CH_2)_nC_{6-12}$ aryl, $-O-(CH_2)_n$(3-12 membered heteroalicyclic), $-O-(CH_2)_n$(5-12 membered heteroaryl) or -CN, and each hydrogen in R^{11} is optionally substituted by one or more groups selected from halogen, -OH, -CN, $-C_{1-12}$ alkyl which may be partially or fully halogenated, $-O-C_{1-12}$ alkyl which may be partially or fully halogenated, -CO, -SO and $-SO_2$;

R^1 and R^2 may be combined together to form a C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heteroalicyclic group;

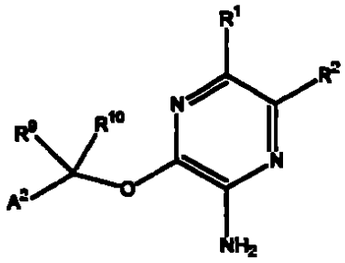
m is 0, 1 or 2;

n is 0, 1, 2, 3 or 4; and

p is 1 or 2;

or a pharmaceutically acceptable salt, solvate or hydrate thereof.

22. The compound of claim 21, wherein the compound has formula 3a



3a

wherein A^2 is C_{6-12} aryl or 5-12 membered heteroaryl optionally substituted by one or more R^3 groups.

23. The compound of claim 22, wherein R^1 is selected from C_{6-12} aryl and 5-12 membered heteroaryl, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

24. The compound of claim 22, wherein R^1 is selected from C_{3-12} cycloalkyl, 3-12 membered heterocalicyclic, $-O(CR^6R^7)_nR^4$, $-C(O)R^4$, $-C(O)OR^4$, $-CN$, $-NO_2$, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-C(O)NR^4R^5$, $-NR^4C(O)R^5$, $-C(=NR^5)NR^4R^5$, C_{1-8} alkyl, C_{2-8} alkenyl, and C_{2-8} alkynyl; and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

25. The compound of claim 22, wherein A^2 is substituted by at least one halogen atom.

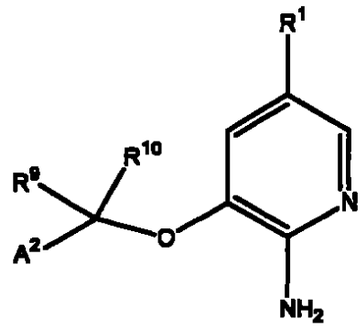
26. The compound of claim 22, wherein R^2 is hydrogen, R^9 and R^{10} are independently C_{1-4} alkyl, and A^2 is phenyl substituted by at least one halogen atom.

27. The compound of claim 21, wherein R^1 is a furan, thiopene, pyrrole, pyrroline, pyrrolidine, dioxolane, oxazole, thiazole, imidazole, imidazoline, imidazolidine, pyrazole, pyrazoline, pyrazolidine, isoxazole, isothiazole, oxadiazole, triazole, thiadiazole, pyran, pyridine, piperidine, dioxane, morpholine, dithiane, thiomorpholine, pyridazine, pyrimidine, pyrazine, piperazine, triazine, trithiane or phenyl group, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

28. The compound of claim 21, wherein R^1 is a fused ring heteroaryl group, and each hydrogen in R^1 is optionally substituted by one or more R^3 groups.

29. The compound of claim 21, wherein R^1 is a $-SO_2NR^4R^5$ group.

30. A compound of formula 4



4

wherein:

R^1 is selected from C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl, 3-12 membered heteroalicyclic, $-O(CR^6R^7)_nR^4$, $-C(O)R^4$, $-C(O)OR^4$, -CN, $-NO_2$, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-C(O)NR^4R^5$, $-NR^4C(O)R^5$, $-C(=NR^5)NR^4R^5$, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl; and each hydrogen in R^1 is optionally substituted by one or more R^3 groups;

R^3 is halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-O(CR^6R^7)_nR^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-C(=NR^5)NR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$, each hydrogen in R^3 is optionally substituted by one or more R^8 groups, and R^3 groups on adjacent atoms may combine to form a C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heteroalicyclic group;

each R^4, R^5, R^6 and R^7 is independently hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl; or any two of R^4, R^5, R^6 and R^7 bound to the same nitrogen atom may, together with the nitrogen to which they are bound, be combined to form a 3 to 12 membered heteroalicyclic or 5-12 membered heteroaryl group optionally containing 1 to 3 additional heteroatoms selected from N, O, and S; or any two of R^4, R^5, R^6 and R^7 bound to the same carbon atom may be combined to form a C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic or 5-12 membered heteroaryl group; and each hydrogen in R^4, R^5, R^6 and R^7 is optionally substituted by one or more R^8 groups;

each R^8 is independently halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, -CN, $-O-C_{1-12}$ alkyl, $-O-(CH_2)_nC_{3-12}$ cycloalkyl, $-O-(CH_2)_nC_{6-12}$ aryl, $-O-(CH_2)_n$(3-12 membered heteroalicyclic) or $-O-(CH_2)_n$(5-12 membered heteroaryl); and each hydrogen in R^8 is optionally substituted by one or more R^{11} groups;

each R^9 and R^{10} is independently hydrogen, halogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, $-S(O)_mR^4$, $-SO_2NR^4R^5$, $-S(O)_2OR^4$, $-NO_2$, $-NR^4R^5$, $-(CR^6R^7)_nOR^4$, -CN, $-C(O)R^4$, $-OC(O)R^4$, $-NR^4C(O)R^5$, $-(CR^6R^7)_nC(O)OR^4$, $-(CR^6R^7)_nNCR^4R^5$, $-NR^4C(O)NR^5R^6$, $-NR^4S(O)_pR^5$ or $-C(O)NR^4R^5$; R^9 and R^{10} may combine to form a C_{3-12} cycloalkyl, 3-12 membered heteroalicyclic, C_{6-12} aryl or 5-12 membered heteroaryl ring; and each hydrogen in R^9 and R^{10} is optionally substituted by one or more R^3 groups;

A^2 is C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heteroalicyclic, and A^2 is optionally substituted by one or more R^3 groups;

each R^{11} is independently halogen, C_{1-12} alkyl, C_{1-12} alkoxy, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, -O-C_{1-12} alkyl, -O-$(CH_2)_nC_{3-12}$ cycloalkyl, -O-$(CH_2)_nC_{6-12}$ aryl, -O-$(CH_2)_n$(3-12 membered heterocalicyclic), -O-$(CH_2)_n$(5-12 membered heteroaryl) or -CN, and each hydrogen in R^{11} is optionally substituted by one or more groups selected from halogen, -OH, -CN, -C_{1-12} alkyl which may be partially or fully halogenated, -O-C_{1-12} alkyl which may be partially or fully halogenated, -CO, -SO and -SO_2;

m is 0, 1 or 2;

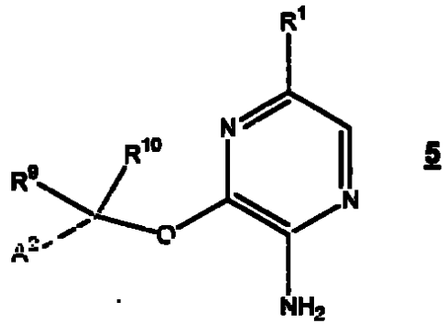
n is 0, 1, 2, 3 or 4; and

p is 1 or 2;

or a pharmaceutically acceptable salt, solvate or hydrate thereof.

31. The compound of claim 30, wherein A^2 is C_{6-12} aryl or 5-12 membered heteroaryl optionally substituted by one or more R^3 groups.

32. A compound of formula 5



5

wherein:

R^1 is selected from C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl, 3-12 membered heterocalicyclic, -$O(CR^6R^7)_mR^4$, -$C(O)R^4$, -$C(O)OR^4$, -CN, -NO_2, -$S(O)_mR^4$, -$SO_2NR^4R^5$, -$C(O)NR^4R^5$, -$NR^4C(O)R^5$, -$C(=NR^6)NR^4R^5$, C_{1-8} alkyl, C_{2-8} alkenyl, and C_{2-8} alkynyl; and each hydrogen in R^1 is optionally substituted by one or more R^3 groups;

R^3 is halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl, -$S(O)_mR^4$, -$SO_2NR^4R^5$, -$S(O)_2OR^4$, -NO_2, -NR^4R^5, -$(CR^6R^7)_nOR^4$, -CN, -$C(O)R^4$, -$OC(O)R^4$, -$O(CR^6R^7)_nR^4$, -$NR^4C(O)R^5$, -$(CR^6R^7)_nC(O)OR^4$, -$(CR^6R^7)_nNCR^4R^5$, -$C(=NR^6)NR^4R^5$, -$NR^4C(O)NR^5R^5$, -$NR^4S(O)_pR^5$ or -$C(O)NR^4R^5$, each hydrogen in R^3 is optionally substituted by one or more R^8 groups, and R^3 groups on adjacent atoms may combine to form a C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heterocalicyclic group;

each R^4, R^5, R^6 and R^7 is independently hydrogen, halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heterocalicyclic, 5-12 membered heteroaryl; or any two of R^4, R^5, R^6 and R^7 bound to the same nitrogen atom may, together with the nitrogen to which they are bound, be combined to form a 3 to 12 membered heterocalicyclic or 5-12 membered heteroaryl group optionally containing 1 to 3 additional heteroatoms selected from N, O, and S; or any two of R^4, R^5, R^6

and R^7 bound to the same carbon atom may be combined to form a C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic or 5-12 membered heteroaryl group; and each hydrogen in R^4, R^5, R^6 and R^7 is optionally substituted by one or more R^8 groups;

each R^8 is independently halogen, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, -CN, -O-C_{1-12} alkyl, -O-$(CH_2)_nC_{3-12}$ cycloalkyl, -O-$(CH_2)_nC_{6-12}$ aryl, -O-$(CH_2)_n$(3-12 membered heteroalicyclic) or -O-$(CH_2)_n$(5-12 membered heteroaryl); and each hydrogen in R^8 is optionally substituted by one or more R^{11} groups;

each R^9 and R^{10} is independently hydrogen, halogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, -$S(O)_mR^4$, -$SO_2NR^4R^5$, -$S(O)_2OR^4$, -NO_2, -NR^4R^5, -$(CR^6R^7)_nOR^4$, -CN, -$C(O)R^4$, -$OC(O)R^4$, -$NR^4C(O)R^5$, -$(CR^6R^7)_nC(O)OR^4$, -$(CR^6R^7)_nNCR^4R^5$, -$NR^4C(O)NR^5R^6$, -$NR^4S(O)_pR^5$ or -$C(O)NR^4R^5$; R^9 and R^{10} may combine to form a C_{3-12} cycloalkyl, 3-12 membered heteroalicyclic, C_{6-12} aryl or 5-12 membered heteroaryl ring; and each hydrogen in R^9 and R^{10} is optionally substituted by one or more R^8 groups;

A^2 is C_{6-12} aryl, 5-12 membered heteroaryl, C_{3-12} cycloalkyl or 3-12 membered heteroalicyclic, and A^2 is optionally subetituted by one or more R^3 groups; except that when R^2, R^9 and R^{10} are all H and A^2 is m-chlorophenyl, R^1 is not unsubstituted piperazine;

each R^{11} is independently halogen, C_{1-12} alkyl, C_{1-12} alkoxy, C_{3-12} cycloalkyl, C_{6-12} aryl, 3-12 membered heteroalicyclic, 5-12 membered heteroaryl, -O-C_{1-12} alkyl, -O-$(CH_2)_nC_{3-12}$ cycloalkyl, -O-$(CH_2)_nC_{6-12}$ aryl, -O-$(CH_2)_n$(3-12 membered heteroalicyclic), -O-$(CH_2)_n$(5-12 membered heteroaryl) or -CN, and each hydrogen in R^{11} is optionally substituted by one or more groups selected from halogen, -OH, -CN, -C_{1-12} alkyl which may be partially or fully halogenated, -O-C_{1-12} alkyl which may be partially or fully halogenated, -CO, -SO and -SO_2;

m is 0, 1 or 2;

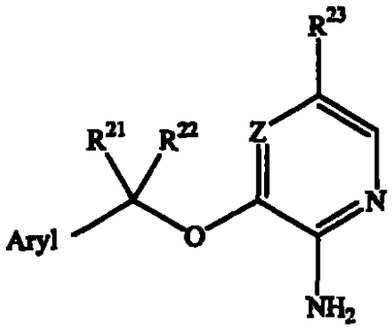
n is 0, 1, 2, 3 or 4; and

p is 1 or 2;

or a pharmaceutically acceptable salt, solvate or hydrate thereof.

33. The compound of claim 32, wherein A^2 is C_{6-12} aryl or 5-12 membered heteroaryl optionally substituted by one or more R^3 groups.

34. A compound of formula 6



(6)

wherein,

Z is CH or N;

Aryl is an optionally fused aryl or an optionally fused heteroaryl group which is optionally substituted by one or more substituents selected from the group consisting of a halogen, $-OR^{24}$, $-COR^{24}$, $-COOR^{24}$, $-CONR^{24}R^{25}$, -CN, $-NO_2$, $-S(O)_mR^{24}$, $-SO_2NR^{24}R^{25}$, perfluoroalkyl, lower alkyl, cycloalkyl, heterocycle, alkenyl, alkynyl, aryl, $-NR^{24}R^{25}$, $-NR^{24}C(O)R^{25}$ and $-NR^{24}S(O)_pR^{25}$;

R^{21} and R^{22} are independently selected from the group consisting of hydrogen, halogen, $-COR^{24}$, $-COOR^{24}$, $-CONR^{24}R^{25}$, -CN, perfluoroalkyl, lower alkyl, cycloalkyl, heterocycle, alkenyl, alkynyl, and aryl;

R^{23} is selected from the group consisting of:

an optionally fused aryl, heteroaryl, alicyclic or heterocyclic group, optionally substituted by one or more substituents selected from the group consisting of a halogen, $-(CH_2)_m-OR^{24}$, $-COR^{24}$, $-COOR^{24}$, $-CONR^{24}R^{25}$, -CN, $-NO_2$, $-S(O)_mR^{24}$, $-SO_2NR^{24}R^{25}$, perfluoroalkyl, -O-perfluoroalkyl, lower alkyl, cycloalkyl, heterocycle, heteroaryl, alkenyl, alkynyl, aryl, $-(CH_2)_m-NR^{24}R^{25}$, $-NR^{24}C(O)R^{25}$ and $-NR^{24}S(O)_pR^{25}$, wherein said heterocycle, heteroaryl and aryl substituents may be optionally substituted by a group selected from the group consisting of lower alkyl, halogen, $-C(O)NR^{24}R^{25}$, $NR^{24}R^{25}$, $NR^{24}C(O)R^{25}$ and $NR^{24}S(O)_pR^{25}$;

$-OR^{24}$, $-COR^{24}$, $-COOR^{24}$, -CN, $-NO_2$, $-S(O)_mR^{24}$, $-SO_2NR^{24}R^{25}$, perfluoroalkyl, cycloalkyl, heterocycle, alkenyl, and alkynyl;

R^{24} and R^{25} are independently selected from the group consisting of hydrogen, lower alkyl, cycloalkyl, alkenyl, alkynyl, aryl, aminoalkyl, alkylaminoalkyl, alkylaminocycloalkyl, dialkylaminoalkyl and $-(CH_2)_m$-heterocycle, wherein said $-(CH_2)_m$-heterocycle may be further substituted by one or more of lower alkyl, $-(CH_2)_m$-hydroxy, heterocycle and $-C(O)R^{26}$,

or R^{24} and R^{25} can combine to form a 5- to 6-membered heterocyclic ring having one or more heteroatoms selected from the group consisting of N, O, S, S(O) and SO_2, said 5- to 6-membered heterocyclic ring may be optionally substituted by lower alkyl, $-(CH_2)_m$-heterocycle, cycloalkyl, halo, $-(CH_2)_m-NR^{26}R^{27}$, amino, $-C(O)R^{26}$, $-NR^{26}-C(O)OR^{27}$ and $-NR^{26}-C(O)R^{27}$;

wherein R^{26} and R^{27} are independently selected from the group consisting of hydrogen, lower alkyl, $-(CH_2)_m$-cycloalkyl and $-C(O)-(CH_2)_m-OH$;

157

except that when Z is N and R^{21} and R^{22} are H and Aryl is m-chlorophenyl, R^{23} is not piperazine;

m is 0, 1 or 2;

n is 0, 1, 2 or 3;

p is 1 or 2;

or a pharmaceutically acceptable salt thereof.

35. The compound of claim 34, wherein R^{23} is aryl or heteroaryl.

36. A compound selected from the group consisting of: 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenol; 3-(2,6-dichloro-benzyloxy)-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-[3-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(1H-indol-4-yl)-pyridin-2-ylamine; 3-[2-chloro-6-(1H-indol-4-yl)-benzyloxy]-5-(1H-indol-4-yl)-pyridin-2-ylamine; 2-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-pyrrole-1-carboxylic acid tert-butyl ester; 3-(2,6-dichloro-benzyloxy)-5-(1H-pyrrol-2-yl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(4-fluoro-phenyl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(2-fluoro-phenyl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(3-fluoro-phenyl)-pyridin-2-ylamine; 5-(4-amino-phenyl)-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine; *N*-[4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl]-methanesulfonamide; N-[4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl]-acetamide; 3-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenol; 3-(2,6-dichloro-benzyloxy)-5-(4-methoxy-phenyl)-pyridin-2-ylamine; 5-(3-amino-phenyl)-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(3-trifluoromethoxy-phenyl)-pyridin-2-ylamine; 2-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenol; 3-(2,6-dichloro-benzyloxy)-5-(2-phenoxy-phenyl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(3,4-difluoro-phenyl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(3-isopropyl-phenyl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(2-trifluoromethyl-phenyl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(2-methoxy-phenyl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(4-trifluoromethyl-phenyl)-pyridin-2-ylamine; *N*-[2-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl]-methanesulfonamide; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-methanol; 5-benzo[1,3]dioxol-5-yl-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(2-trifluoromethoxy-phenyl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(4-methyl-thiophen-2-yl)-pyridin-2-ylamine; 5-(2-benzyloxy-phenyl)-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(3-methoxy-phenyl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-6-(1*H*-indol-2-yl)-pyridin-2-ylamine; 5-(4-benzyloxy-3-fluoro-phenyl)-3-(2,6-dichloro-benzyloxy)-pyridin-2-ylamine; 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid; 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-N-(2-diethylamino-ethyl)-benzamide; 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-N-(3-diethylamino-propyl)-benzamide; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {4-[6-amino-5-(2,6-

dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[4-(2-hydroxy-ethyl)-piperidin-1-yl]-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*R*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-cyclopropylaminomethyl-piperidin-1-yl]-methanone; 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-*N*-(2-hydroxy-3-pyrrolidin-1-yl-propyl)-benzamide; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-(3-fluoro-piperidin-1-ylmethyl)-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-cyclopropyl-piperazin-1-yl)-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2R)-2-[(cyclopropylmethyl-amino)-methyl]-pyrrolidin-1-yl]-methanone; 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-N-cyclopropylmethyl-*N*-(2*R*)-pyrrolidin-2-ylmethyl-benzamide; 4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-N-(2-hydroxy-3-pyrrolidin-1-yl-propyl)-N-methyl-benzamide; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-[(3*R*)-3-hydroxy-pyrrolidin-1-ylmethyl]-pyrrolidin-1-yl]-methanone; 3-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid; {3-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenoxy}-acetic acid; 2-{4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenoxy}-1-[(2R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-ethanone; 2-{4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenoxy}-1-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-ethanone; 3-(2,6-dichloro-benzyloxy)-5-(1H-indol-5-yl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-[3-(1-methyl-1,2,3,6-tetrahydro-pyridin-4-yl)-1H-indol-5-yl]-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-[3-(1-methyl-piperidin-4-yl)-1*H*-indol-5-yl]-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(3-morpholin-4-ylmethyl-1*H*-indol-5-yl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(3-piperidin-1-ylmethyl-1*H*-indol-5-yl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(3-pyrrolidin-1-ylmethyl-1*H*-indol-5-yl)-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-(3-diethylaminomethyl-1H-indol-5-yl)-pyridin-2-ylamine; (1-{5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-3-ylmethyl}-(3*R*)-pyrrolidin-3-yl)-carbamic acid *tert*-butyl ester; 3-(2,6-dichloro-benzyloxy)-5-[3-(2,6-dimethyl-morpholin-4-ylmethyl)-1*H*-indol-5-yl]-pyridin-2-ylamine; *N*-(1-{5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-3-ylmethyl}-(3*R*)-pyrrolidin-3-yl)-acetamide; 1-(4-{5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-3-ylmethyl}-piperazin-1-yl)-ethanone; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(1*H*-indol-5-yl)-pyridin-2-ylamine; 1-(4-{5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-1*H*-indol-3-ylmethyl}-piperazin-1-yl)-ethanone; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-[3-(2,6-dimethyl-morpholin-4-ylmethyl)-1*H*-indol-5-yl]-pyridin-2-ylamine; *N*-(1-{5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-1*H*-indol-3-ylmethyl}-(3*S*)-pyrrolidin-3-yl)-acetamide; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(3-piperidin-1-ylmethyl-1*H*-indol-5-yl)-pyridin-2-ylamine; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(3-morpholin-4-ylmethyl-1*H*-indol-5-yl)-pyridin-2-ylamine; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(3-pyrrolidin-1-ylmethyl-1*H*-indol-6-yl)-pyridin-2-ylamine; 5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carboxylic acid ethyl ester; 5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carboxylic acid; {5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-2-yl}-(4-methyl-piperazin-1-yl)-methanone; {5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-2-yl}-[(3*R*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-2-yl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-

pyrrolidin-1-yl]-methanone; 5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carboxylic acid (2-pyrrolidin-1-yl-ethyl)-amide; 5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carboxylic acid (2-morpholin-4-yl-ethyl)-amide; (1-{5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carbonyl}-(3*S*)-pyrrolidin-3-yl)-carbamic acid *tert*-butyl ester; {5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indol-2-yl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone; 5-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-1*H*-indole-2-carboxylic acid (2-hydroxy-3-pyrrolidin-1-yl-propyl)-amide; 4-(6-amino-5-benzyloxy-pyridin-3-yl)-phenol; 3-benzyloxy-5-phenyl-pyridin-2-ylamine; 3-(3-methoxy-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2-chloro-4-fluoro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2-chloro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2,5-dichloro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2-chloro-5-trifluoromethyl-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2,4-dichloro-5-fluoro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2-chloro-3-trifluoromethyl-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(3,4-dichloro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 2-(2-amino-5-phenyl-pyridin-3-yloxymethyl)-benzonitrile; 3-(2-chloro-6-fluoro-3-methyl-benzyloxy)-5-phenyl-pyridin-2-ylamine; 5-Phenyl-3-(2,3,6-trifluoro-benzyloxy)-pyridin-2-ylamine; 3-(2,6-difluoro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2,6-difluoro-3-methyl-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(3-chloro-2,6-difluoro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(2-chloro-6-fluoro-benzyloxy)-5-phenyl-pyridin-2-ylamine; 3-(3-Fluoro-4-methoxy-benzyloxy)-5-phenyl-pyridin-2-ylamine; *N*-[3-(2-amino-5-phenyl-pyridin-3-yloxymethyl)-phenyl]-methanesulfonamide; 5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-3-(3-nitro-benzyloxy)-pyridin-2-ylamine; 5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-3-(naphthalen-1-ylmethoxy)-pyridin-2-ylamine; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 2-[2-amino-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-3-yloxy]-*N*-(4-isopropyl-phenyl)-2-phenyl-acetamide; 3-(5-chloro-benzo[*b*]thiophen-3-ylmethoxy)-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine; {4-[6-amino-5-(4-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-fluoro-6-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(5-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; (4-[6-amino-5-[1-(2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; [4-[6-amino-5-(2-bromo-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; 4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenol; 3-(2,6-difluoro-benzyloxy)-5-(1H-indol-4-yl)-pyridin-2-ylamine; 3-(2,6-difluoro-benzyloxy)-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid; {4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenoxy}-acetic acid ethyl ester; {4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenoxy}-acetic acid; 2-[4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenoxy]-1-[(2R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-ethanone; 2-{4-[6-amino-5-(2,6-difluoro-

benzyloxy)-pyridin-3-yl]-phenoxy}-1-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-ethanone; 4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-phenol; 4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-phenol; 4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenol; 2-[2-amino-5-(4-hydroxy-phenyl)-pyridin-3-yloxymethyl]-benzonitrile; 4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenol; 4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenol; 4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-phenol; *N*-{4-[6-amino-5-(2-cyano-benzyloxy)-pyridin-3-yl]-phenyl}-methanesulfonamide; 2-[2-amino-5-(4-methanesulfonylamino-phenyl)-pyridin-3-yloxymethyl]-benzamide; 2-[2-amino-5-(4-methanesulfonylamino-phenyl)-pyridin-3-yloxymethyl]-benzoic acid; *N*-(4-[6-amino-5-[2-(4-methyl-piperazine-1-carbonyl)-benzyloxy]-pyridin-3-yl]-phenyl)-methanesulfonamide; 2-[2-amino-5-(4-methanesulfonylamino-phenyl)-pyridin-3-yloxymethyl]-*N*-(2-hydroxy-ethyl)-benzamide; 2-[2-amino-5-(4-methanesulfonylamino-phenyl)-pyridin-3-yloxymethyl]-*N*-isobutyl-benzamide; 4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-benzoic acid; {4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; 1-(4-{4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-benzoyl}-piperazin-1-yl)-ethanone; 4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 4-[6-amino-5-(2-chloro-6-fluoro-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; 4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-benzoic acid; {4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; 1-(4-{4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-benzoyl}-piperazin-1-yl)-ethanone; 4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 4-[6-amino-5-(2-chloro-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; 4-[6-amino-5-(2-cyano-benzyloxy)-pyridin-3-yl]-benzoic acid; 2-[2-amino-5-[4-((2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl]-benzonitrile; 2-[2-amino-5-[4-((2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl]-benzonitrile; 2-[2-amino-5-[4-((3*S*)-3-dimethylamino-pyrrolidine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl]-benzonitrile; 2-[2-amino-5-[4-((3*S*)-3-amino-pyrrolidine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl]-benzonitrile; 2-[2-amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl]-benzonitrile; 2-[2-amino-5-[4-(4-methyl-piperazine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl]-benzonitrile; 2-[5-[4-(4-acetyl-piperazine-1-carbonyl)-phenyl]-2-amino-pyridin-3-yloxymethyl]-benzonitrile; 4-[6-amino-5-(2-cyano-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; 4-[6-amino-5-(2-cyano-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 4-[6-

amino-5-(2-cyano-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; 4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-benzoic acid; {4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; 1-(4-{4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-benzoyl}-piperazin-1-yl)-ethanone; 4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; 4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 4-[6-amino-5-(2,4-dichloro-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; 4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-benzoic acid; {4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(3S)-3-dimethylamino-pyrrolidin-1-yl]-methanone; [(3*S*)-3-amino-pyrrolidin-1-yl]-{4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-methanone; {4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; 1-(4-{4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-benzoyl}-piperazin-1-yl)-ethanone; 4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; 4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 4-[6-amino-5-(2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; 4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-benzoic acid; {4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(3R)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; 1-(4-{4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-benzoyl}-piperazin-1-yl)-ethanone; 4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; 4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 4-[6-amino-5-(4-*tert*-butyl-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; 4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-benzoic acid; {4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3S)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; 1-(4-{4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-benzoyl}-piperazin-1-yl)-ethanone; 4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-

pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 4-[6-amino-5-(2-chloro-4-fluoro-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid; {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-amino-piperidin-1-yl)-methanone; {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone; {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*R*)-3-amino-pyrrolidin-1-yl]-methanone; {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone; 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(2-pyrrolidin-1-yl-ethyl)-benzamide; 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(3-pyrrolidin-1-yl-propyl)-benzamide; 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; 3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzoic acid; {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-amino-piperidin-1-yl)-methanone; {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone; {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*R*)-3-amino-pyrrolidin-1-yl]-methanone; {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-[(3*S*)-amino-pyrrolidin-1-yl]-methanone; 3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; 3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(2-pyrrolidin-1-yl-ethyl)-benzamide; 3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(3-pyrrolidin-1-yl-propyl)-benzamide; 3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; *N*-[2-(4-acetyl-piperazin-1-yl)-ethyl]-3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-benzamide; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-[4-(1,1-dioxo-1λ^6-isothiazolidin-2-yl)-phenyl]-pyridin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-[4-(1,1-dioxo-1λ^6-isothiazolidin-2-yl)-phenyl]-pyridin-2-ylamine; 5-[4-(1,1-dioxo-1λ^6-isothiazolidin-2-yl)-phenyl]-3-(2-fluoro-6-trifluoromethyl-benzyloxy)-pyridin-2-ylamine; 2-diethylamino-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-cyclopropylamino-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-Pyrrolidin-1-yl-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-(4-hydroxy-piperidin-1-yl)-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-

160

pyridin-3-yl]-phenyl}-amide; 2-morpholin-4-yl-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-Piperidin-1-yl-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-dimethylamino-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-(4-acetyl-piperazin-1-yl)-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-(cyclopropylmethyl-amino)-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-[(3*R*)-3-hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-[(2S)-2-hydroxymethyl-pyrrolidin-1-yl]-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-[4-(2-hydroxy-acetyl)-piperazin-1-yl]-ethanesulfonic acid {4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-(4-acetyl-piperazin-1-yl)-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-Pyrrolidin-1-yl-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-morpholin-4-yl-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-diethylamino-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-dimethylamino-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-Piperidin-1-yl-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-[(3*R*)-3-hydroxymethyl-pyrrolidin-1-yl]-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-(4-hydroxy-piperidin-1-yl)-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-[4-(2-hydroxy-acetyl)-piperazin-1-yl]-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-[(3*R*)-3-hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-(cyclopropylmethyl-amino)-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 2-cyclopropylamino-ethanesulfonic acid {3-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-amide; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(2-dimethylaminomethyl-phenyl)-pyridin-2-ylamine; compound with trifluoro-acetic acid; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(3-pyrrolidin-1-yl-phenyl)-pyridin-2-ylamine; compound with trifluoro-acetic acid; *N*-{4-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-methanesulfonamide; compound with trifluoro-acetic acid; 5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophene-2-carboxylic acid; {5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophen-2-yl}-(4-methyl-piperazin-1-yl)-methanone; {5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophen-2-yl}-[(2R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; 5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophene-2-carboxylic acid (1-methyl-piperidin-4-yl)-amide; {5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophen-2-yl}-(3,5-dimethyl-piperazin-1-yl)-methanone; 5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophene-2-carboxylic acid (2-pyrrolidin-1-yl-ethyl)-amide; {5-[6-amino-5-(2-chloro-3,6-difluoro-benzyloxy)-pyridin-3-yl]-thiophen-2-yl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-benzoic acid; {4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; {4-[6-amino-

5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone; {4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-(3-dimethylamino-pyrrolidin-1-yl)-methanone; {4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; 4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; {4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; *N*-[2-(4-acetyl-piperazin-1-yl)-ethyl]-4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-benzamide; 2-Piperidin-1-yl-ethanesulfonic acid (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide; 2-(4-hydroxy-piperidin-1-yl)-ethanesulfonic acid (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide; 2-dimethylamino-ethanesulfonic acid (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide; 2-cyclopropylamino-ethanesulfonic acid (4-[6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide; 4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; 4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-[(3*R*)-3-amino-pyrrolidin-1-yl)]-methanone; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(3,5-dimethyl-piperazin-1-yl)-methanone; 2-cyclopropylamino-ethanesulfonic acid (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide; 2-dimethylamino-ethanesulfonic acid (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide; 2-[(3*R*)-3-hydroxy-pyrrolidin-1-yl)]-ethanesulfonic acid (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-amide; and pharmaceutically acceptable salts, hydrates and solvates thereof.

37. A compound selected from the group consisting of: 4-[5-amino-6-(2,6-dichloro-benzyloxy)-pyrazin-2-yl]-phenol; 3-(2,6-dichloro-benzyloxy)-5-[4-(1,1-dioxo-1λ^6-isothiazolidin-2-yl)-phenyl]-pyrazin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-[3-(2-morpholin-4-yl-ethoxy)-phenyl]-pyrazin-2-ylamine; 3-(2,6-dichloro-benzyloxy)-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyrazin-2-ylamine; 5-(4-amino-phenyl)-3-(2,6-dichloro-benzyloxy)-pyrazin-2-ylamine; 4-[5-amino-6-(2,6-dichloro-benzyloxy)-pyrazin-2-yl]-benzoic acid; {4-[5-amino-6-(2,6-dichloro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; {4-[5-amino-6-(2,6-dichloro-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 2-morpholin-4-yl-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-piperidin-1-yl-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-pyrrolidin-1-yl-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-[(3*R*)-3-Hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-[(2*S*)-2-Hydroxymethyl-pyrrolidin-1-yl]-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-

161

benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-(cyclopropylmethyl-amino)-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-dimethylamino-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-diethylamino-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-(4-acetyl-piperazin-1-yl)-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-[4-(2-Hydroxy-acetyl)-piperazin-1-yl]-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-cyclopropylamino-ethanesulfonic acid {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-[(3*R*)-3-Hydroxymethyl-pyrrolidin-1-yl]-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-(4-acetyl-piperazin-1-yl)-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-piperidin-1-yl-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-diethylamino-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-morpholin-4-yl-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-pyrrolidin-1-yl-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-dimethylamino-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-[4-(2-Hydroxy-acetyl)-piperazin-1-yl]-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-(cyclopropylmethyl-amino)-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-[(3*R*)-3-Hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 2-cyclopropylamino-ethanesulfonic acid {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-amide; 4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-benzoic acid; {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; 4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(2-pyrrolidin-1-yl-ethyl)-benzamide; {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone; *N*-[2-(4-acetyl-piperazin-1-yl)-ethyl]-4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-benzamide; 4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(3-pyrrolidin-1-yl-propyl)-benzamide; {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(3*R*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone; {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; 4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; 4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; {4-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; 3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-benzoic acid; {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; {3-[5-amino-6-(2-chloro-3,6-

difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(3*R*)-3-amino-pyrrolidin-1-yl]-methanone; {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(3*S*)-3-amino-pyrrolidin-1-yl]-methanone; {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone; 3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(3-morpholin-4-yl-propyl)-benzamide; {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(3*S*)-3-dimethylamino-pyrrolidin-1-yl]-methanone; 3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(2-pyrrolidin-1-yl-ethyl)-benzamide; 3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; {3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-phenyl}-[(2*S*)-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl]-methanone; 3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; *N*-[2-(4-acetyl-piperazin-1-yl)-ethyl]-3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-benzamide; 3-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-*N*-(3-pyrrolidin-1-yl-propyl)-benzamide; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(1*H*-indol-5-yl)-pyrazin-2-ylamine; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(3-pyrrolidin-1-ylmethyl-1*H*-indol-5-yl)-pyrazin-2-ylamine; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(3-diethylaminomethyl-1*H*-indol-5-yl)-pyrazin-2-ylamine; 1-(4-{5-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-1*H*-indol-3-ylmethyl}-piperazin-1-yl)-ethanone; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-[3-(2,6-dimethyl-morpholin-4-ylmethyl)-1*H*-indol-5-yl]-pyrazin-2-ylamine; *N*-(1-{5-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-1*H*-indol-3-ylmethyl}-(3*S*)-pyrrolidin-3-yl)-acetamide; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(3-piperidin-1-ylmethyl-1*H*-indol-5-yl)-pyrazin-2-ylamine; 3-(2-chloro-3,6-difluoro-benzyloxy)-5-(3-morpholin-4-ylmethyl-1*H*-indol-5-yl)-pyrazin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-2-methyl-propoxy]-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyrazin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyrazin-2-ylamine; compound with trifluoro-acetic acid; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyrazin-2-ylamine; compound with trifluoro-acetic acid; *N*-(4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-methanesulfonamide; 2-pyrrolidin-1-yl-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-piperidin-1-yl-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-(cyclopropylmethyl-amino)-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-[(3*R*)-3-Hydroxy-pyrrolidin-1-yl]-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-[(2*S*)-2-Hydroxymethyl-pyrrolidin-1-yl]-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-dimethylamino-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-morpholin-4-yl-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-diethylamino-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-cyclopropylamino-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-benzoic acid; (3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-

162

phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-[(3*S*)-3-amino-pyrrolidin-1-yl)-m-ethanone; (3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-[(3*R*)-3-amino-pyrrolidin-1-yl)-m-ethanone; (3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-[(2*R*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; *N*-[2-(4-acetyl-piperazin-1-yl)-ethyl]-3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-benzamide; (3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-[(2*S*)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; 3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-benzoic acid; 3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-*N*-(1-methyl-piperidin-4-yl)-benzamide; 3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-*N*-(3-pyrrolidin-1-yl-propyl)-benzamide; (3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 4-{5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl}-benzoic acid; 4-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-*N*-(2-morpholin-4-yl-ethyl)-benzamide; 4-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-*N*-(1-methyl-piperidin-4-yl)-benzamide; and pharmaceutically acceptable salts, hydrates and solvates thereof.

38. A compound selected from the group consisting of: (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; N-[2-(4-acetyl-piperazin-1-yl)-ethyl]-4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-benzamide; 4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide; 4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-amino-piperidin-1-yl)-methanone; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((S)-3-hydroxy-pyrrolidin-1-yl)-methanone; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((R)-3-hydroxy-pyrrolidin-1-yl)-methanone; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((R)-2-hydroxymethyl-pyrrolidin-1-yl)-methanone; 4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-diethylamino-ethyl)-benzamide; 4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; 3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-benzoic acid; (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; 3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; N-[2-(4-acetyl-piperazin-1-yl)-ethyl]-3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-benzamide; (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone; 3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(3-morpholin-4-yl-propyl)-benzamide; (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; 3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; 3-{6-

amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide; 3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 2-diethylamino-ethanesulfonic acid (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 2-piperidin-1-yl-ethanesulfonic acid (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 2-(cyclopropylmethyl-amino)-ethanesulfonic acid (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 2-((R)-3-Hydroxy-pyrrolidin-1-yl)-ethanesulfonic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 2-cyclopropylamino-ethanesulfonic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 2-diethylamino-ethanesulfonic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-benzoic acid; 4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; 4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone; (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide; (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone; 3-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-benzoic acid; (3-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; (3-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone; 3-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; (3-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; 3-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide; 3-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; (3-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone; 3-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; (3-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (3-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-[3-(2-

163

morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(4-[2-(1-methyl-pyrrolidin-2-yl)-ethoxy]-phenyl}-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[3-(2-morpholin-4-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 1-(4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenoxy)-3-morpholin-4-yl-propan-2-ol; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(2-diethylamino-ethoxy)-phenyl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(1-methyl-piperidin-3-ylmethoxy)-phenyl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(2-diisopropylamino-ethoxy)-phenyl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(1-methyl-piperidin-4-yloxy)-phenyl]-pyridin-2-ylamine; N-(4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-methanesulfonamide; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-[4-(1,1-dioxo-1lambda*6*-isothiazolidin-2-yl)-phenyl]-pyridin-2-ylamine; N-(4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-methanesulfonamide; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-phenyl-pyridin-2-ylamine; N-(4-{6-amino-5-[(R)-1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-methanesulfonamide; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-thiophen-3-yl-pyridin-2-ylamine; 5-benzo[b]thiophen-2-yl-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 4-methyl-piperazine-1-carboxylic acid (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 1-(4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(2-pyrrolidin-1-yl-ethyl)-urea; 1-(4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(2-hydroxy-ethyl)-urea; 1-(4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(2-morpholin-4-yl-ethyl)-urea; (R)-3-amino-pyrrolidine-1-carboxylic acid (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; (S)-3-amino-pyrrolidine-1-carboxylic acid (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 1-(4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(1-methyl-piperidin-4-yl)-urea; 1-(4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(1-methyl-piperidin-4-yl)-urea; (R)-3-amino-pyrrolidine-1-carboxylic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; (S)-3-amino-pyrrolidine-1-carboxylic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 1-(4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(2-hydroxy-ethyl)-urea; 4-methyl-piperazine-1-carboxylic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 1-(4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(2-pyrrolidin-1-yl-ethyl)-urea; 1-(4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-3-(2-morpholin-4-yl-ethyl)-urea; (R)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-amide; 3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-benzoic acid; (3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; (3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; 3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; (3-{6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((S)-2-pyrrolidin-1-

ylmethyl-pyrrolidin-1-yl)-methanone; 3-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide; N-[2-(4-acetyl-piperazin-1-yl)-ethyl]-3-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-benzamide; 3-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-N-(1-methyl-piperidin-4-yl)-benzamide; (3-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (3-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (3-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone; (3-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone; 4-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid; 4-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; 4-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-N-(2-morpholin-4-yl-ethyl)-benzamide; (4-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; 4-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-N-(1-methyl-piperidin-4-yl)-benzamide; (4-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; N-[2-(4-acetyl-piperazin-1-yl)-ethyl]-4-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-benzamide; 4-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide; (4-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((S)-3-aminopyrrolidin-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; (4-[6-amino-5-[1-(2,6-dichloro-phenyl)-ethoxy]-pyridin-3-yl]-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (S)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-amide; 4-methyl-piperazine-1-carboxylic acid (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-amide; 4-pyrrolidin-1-yl-piperidine-1-carboxylic acid (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-amide; (3R,5S)-3,5-dimethyl-piperazine-1-carboxylic acid (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-amide; 1-(3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-3-(1-methyl-piperidin-4-yl)-urea; 1-(3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-3-(3-pyrrolidin-1-yl-propyl)-urea; 1-(3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-3-(2-pyrrolidin-1-yl-ethyl)-urea; 1-(3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-3-(2-morpholin-4-yl-ethyl)-urea; 1-(3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-3-(3-morpholin-4-yl-propyl)-urea; (R)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-amide; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-dimethylamino-prop-1-ynyl)-pyridin-2-ylamine; (3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-urea; N-(3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-2-piperidin-1-yl-acetamide; N-(3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-2-morpholin-4-yl-acetamide; N-(3-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl]-prop-2-ynyl)-2-pyrrolidin-1-yl-acetamide; N-(3-[6-amino-5-[1-(2,6-

dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-2-((R)-3-hydroxy-pyrrolidin-1-yl)-acetamide; N-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-2-(4-hydroxy-piperidin-1-yl)-acetamide; N-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-2-dimethylamino-acetamide; N-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-prop-2-ynyl)-2-diethylamino-acetamide; 2-(4-acetyl-piperazin-1-yl)-N-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]pyridin-3-yl}-prop-2-ynyl)-acetamide; 4-methyl-piperazine-1-carboxylic acid (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-1,1-dimethyl-prop-2-ynyl)-amide; (3R,5S)-3,5-dimethyl-piperazine-1-carboxylic acid (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-1,1-dimethyl-prop-2-ynyl)-amide; (R)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-1,1-dimethyl-prop-2-ynyl)-amide; (S)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-1,1-dimethyl-prop-2-ynyl)-amide; 1-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-1,1-dimethyl-prop-2-ynyl)-3-(2-morpholin-4-yl-ethyl)-urea; 1-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-1,1-dimethyl-prop-2-ynyl)-3-(2-pyrrolidin-1-yl-ethyl)-urea; 4-pyrrolidin-1-yl-piperidine-1-carboxylic acid (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-1,1-dimethyl-prop-2-ynyl)-amide; 3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-propynoic acid cyclohexylamide; 3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-propynoic acid isopropylamide; 4-(3-amino-3-methyl-but-1-ynyl)-2-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-phenylamine; (4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1yl)-methanone; (4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; (4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; 4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; 4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; 4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; 4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide; 4-{6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-N-(3-morpholin-4-yl-propyl)-benzamide; 6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-nicotinonitrile; 6-amino-5-[1-(2,6-dichloro-3-cyano-phenyl)-ethoxy]-nicotinonitrile; 5-aminomethyl-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; (R)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid {6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-ylmethyl}-amide; N-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-ylmethyl}-methanesulfonamide; N-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-ylmethyl}-acetamide; N-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-ylmethyl}-4-methyl-benzenesulfonamide; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-vinyl-pyridin-2-ylamine; (S)-1-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-ethane-1,2-diol; (R)-1-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-ethane-1,2-

diol; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(1H-pyrazol-4-yl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[1-(2-pyrrolidin-1-yl-ethyl)-1H-pyrazol-4-yl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[1-(2-diisopropylamino-ethyl)-1H-pyrazol-4-yl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[1-(2-morpholin-4-yl-ethyl)-1H-pyrazol-4-yl]-pyridin-2-ylamine; 5-bromo-3-(3-fluoro-2-methoxy-benzyloxy)-pyridin-2-ylamine; 5-bromo-3-[1-(3-fluoro-2-methoxy-phenyl)-ethoxy]-pyridin-2-ylamine; {4-[6-amino-5-(3-fluoro-2-methoxy-benzyloxy)-pyridin-3-yl]-phenyl}-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; (4-[6-amino-5-[1-(3-fluoro-2-methoxy-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 5-bromo-3-(3-fluoro-2-isopropoxy-benzyloxy)-pyridin-2-ylamine; {4-[6-amino-5-(3-fluoro-2-isopropoxy-benzyloxy)-pyridin-3-yl]-phenyl}-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 5-(4-amino-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenoxy)-acetic acid methyl ester; (4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenoxy)-acetic acid; 2-(4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenoxy)-1-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-ethanone; 2-(4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenoxy)-1-((R)-3-hydroxy-pyrrolidin-1-yl)-ethanone; 4-[2-(4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenoxy)-acetyl]-piperazine-1-carboxylic acid tert-butyl ester; 2-(4-[6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenoxy)-1-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-ethanone; 5-bromo-3-(3-fluoro-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-yloxy)-pyridin-2-ylamine; {4-[6-amino-5-(3-fluoro-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-yloxy)-pyridin-3-yl]-phenyl}-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 3-(3-fluoro-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-yloxy)-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-pyridin-2-ylamine; N-{4-[6-amino-5-(3-fluoro-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-yloxy)-pyridin-3-yl]-phenyl}-methanesulfonamide; 3-(3-fluoro-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-yloxy)-5-(1H-pyrazol-4-yl)-pyridin-2-ylamine; 5-bromo-3-[1-(2-chloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 3-[1-(2-chloro-3-fluoro-phenyl)-ethoxy]-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-pyridin-2-ylamine; 5'-benzyloxy-[2,3']bipyridinyl-6'-ylamine; 5-benzyloxy-[3,3']bipyridinyl-6-ylamine; 3-benzyloxy-5-pyrimidin-5-yl-pyridin-2-ylamine; 5-benzyloxy-[3,3']bipyridinyl-6,6'-diamine; 5'-(2-chloro-benzyloxy)-[2,3']bipyridinyl-6'-ylamine; 5-(2-chloro-benzyloxy)-[3,3']bipyridinyl-6-ylamine; 3-(2-chloro-benzyloxy)-5-pyrimidin-5-yl-pyridin-2-ylamine; 5-(2-chloro-benzyloxy)-[3,3']bipyridinyl-6,6'-diamine; 5'-(4-chloro-benzyloxy)-[2,3']bipyridinyl-6'-ylamine; 5-(4-chloro-benzyloxy)-[3,3']bipyridinyl-6-ylamine; 3-(4-chloro-benzyloxy)-5-pyrimidin-5-yl-pyridin-2-ylamine; 5-(4-chloro-benzyloxy)-[3,3']bipyridinyl-6,6'-diamine; 5'-(2-chloro-3,6-difluoro-benzyloxy)-[2,3']bipyridinyl-6'-ylamine; 5-(2-chloro-3,6-difluoro-benzyloxy)-[3,3']bipyridinyl-6-ylamine; 5-(2-chloro-3,6-difluoro-benzyloxy)-[3,4']bipyridinyl-6-ylamine; 3-(2-chloro3,6-difluoro-benzyloxy)-5-pyrimidin-5-yl-pyridin-2-ylamine; 5-(2-chloro-3,6-difluoro-benzyloxy)-[3,3']bipyridinyl-6,6'-diamine; 5'-(2,6-dichloro-benzyloxy)-[2,3']bipyridinyl-6'-ylamine; 5-(2,6-dichloro-benzyloxy)-[3,3']bipyridinyl-6-ylamine; 5-(2,6-dichloro-benzyloxy)-[3,4']bipyridinyl-6-ylamine; 3-(2,6-dichloro-benzyloxy)-5-pyrimidin-5-yl-pyridin-2-ylamine; 5-(2,6-dichloro-benzyloxy)-[3,3']bipyridinyl-6,6'-diamine; 5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6,6'-diamine; {6'-amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-4-yl}-(4-methyl-piperazin-1-yl)-methanone; {6'-amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-

ethoxy]-[2,3']bipyridinyl-6-yl}-(4-methyl-piperazin-1-yl)-methanone; {6'-amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-5-yl}-(4-methyl-piperazin-1-yl)-methanone; {6'-amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6-yl}-(4-methyl-piperazin-1-yl)-methanone; {6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[3,4']bipyridinyl-2'-yl}-(4-methyl-piperazin-1-yl)-methanone; 5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6,6'-diamine; {6'-amino-5'-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-5-yl}-(4-methyl-piperazin-1-yl)-methanone; {6'-amino-5'-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-4-yl}-(4-methyl-piperazin-1-yl)-methanone; {6'-amino-5'-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-6-yl}-(4-methyl-piperazin-1-yl)-methanone; {6'-amino-5'-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-5-yl}-(4-methyl-piperazin-1-yl)-methanone; {6'-amino-5'-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6-yl}-(4-methyl-piperazin-1-yl)-methanone; {6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[3,4']bipyridinyl-2'-yl}-(4-methyl-piperazin-1-yl)-methanone; 5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-6'-ylamine; 5'-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-6'-ylamine; 5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-pyrimidin-5-yl-pyridin-2-ylamine; {6'-amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[2,3']bipyridinyl-5-yl}-(4-methyl-piperazin-1-yl)-methanone; 5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-[3,4']bipyridinyl-6-ylamine; 5-benzyloxy-3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-(2-ethyl-butoxy)-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-(3-methyl-butoxy)-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-butoxy-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-propoxy-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-cyclohexylmethoxy-pyridin-2-ylamine; 6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-ol; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-(2-cyclohexyl-ethoxy)-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-isobutoxy-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-phenethyloxy-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-(pyridin-2-ylmethoxy)-pyridin-2-ylamine; 3-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-5-(pyridin-4-ylmethoxy)-pyridin-2-ylamine; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 5-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-2-fluoro-benzonitrile; 4-(4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-piperidin-4-ol; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-piperidin-1-yl-methanone; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-pyrrolidin-1-yl-methanone; 4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-3-methyl-benzoic acid methyl ester; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(dimethyl-piperazin-1-ylmethyl)-phenyl]-pyridin-2-ylamine; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-3,5-dimethoxy-phenyl)-(dimethyl-piperazin-1-yl)-methanone; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-2-fluoro-phenyl)-(dimethyl-piperazin-1-yl)-methanone; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-3-fluoro-phenyl)-(dimethyl-piperazin-1-yl)-methanone; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-3-methyl-phenyl)-(dimethyl-piperazin-1-yl)-methanone; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-

(4-methyl-[1,4]diazepan-1-yl)-methanone; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-[1,4]diazepan-1-yl-methanone; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-piperazin-1-yl-methanone; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-vinyl-pyridin-2-ylamine; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,4S)-3,4-dihydroxy-pyrrolidin-1-yl)-methanone; 5-[(1-benzyl-pyrrolidin-3-ylamino)-methyl]-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-N-azetidin-3-yl-benzamide; 4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-N,N-dimethyl-benzenesulfonamide; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(6-methoxy-1H-benzoimidazol-2-yl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(6-methoxy-1-methyl-1H-benzoimidazol-2-yl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-(4-methyl-[1,4]diazepane-1-sulfonyl)-phenyl]-pyridin-2-ylamine; 6-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-1-methyl-1H-indazole-3-carboxylic acid amide; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(1-methyl-1H-pyrazol-4-yl)-pyridin-2-ylamine; 5-(3-chloro-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(4-fluoro-3-methyl-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-trifluoromethyl-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-fluoro-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-trifluoromethoxy-phenyl)-pyridin-2-ylamine; 5-benzo[1,3]dioxol-5-yl-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenol; (3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-methanol; 3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-benzonitrile; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-methoxy-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3,5-dichloro-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2,5-dimethyl-phenyl)-pyridin-2-ylamine; 5-(5-chloro-2-methoxy-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 5-(3-chloro-4-fluoro-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(5-fluoro-2-methoxy-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-isopropyl-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3,4-dichloro-phenyl)-pyridin-2-ylamine; 4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-benzonitrile; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3,4-difluoro-phenyl)-pyridin-2-ylamine; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((2R,6S)-2,6-dimethyl-morpholin-4-yl)-methanone; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2-ethoxy-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2,5-dimethoxy-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2,4-dimethoxy-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2,6-dimethoxy-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2-trifluoromethyl-phenyl)-pyridin-2-ylamine; 5-(2-chloro-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2-trifluoromethoxy-phenyl)-pyridin-2-ylamine; 1-(2-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-ethanone; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2-fluoro-phenyl)-pyridin-2-ylamine; (2-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-methanol; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-

166

ethoxy]-5-o-tolyl-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2-methoxy-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2,6-dimethyl-phenyl)-pyridin-2-ylamine; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-morpholin-4-yl-methanone; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-2-chloro-phenyl)-((3R,5S)-dimethyl-piperazin-1-yl)-methanone; 4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-2-methyl-phenyl)-((3R,5S)-dimethyl-piperazin-1-yl)-methanone; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-[4-((2R,6S)-2,6-dimethyl-morpholin-4-ylmethyl)-phenyl]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(4-morpholin-4-ylmethyl-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3,5-dimethyl-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-m-tolyl-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3,4-dimethoxy-phenyl)-pyridin-2-ylamine; 5-biphenyl-3-yl-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 5-(3,5-bis-trifluoromethyl-phenyl)-3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3,4-dichloro-phenyl)-pyridin-2-ylamine; 1-(3-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-ethanone; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3,5-difluoro-phenyl)-pyridin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(2,6-dichloro-phenyl)-pyridin-2-ylamine; (4-{6-amino-5-[1-(2,6-dichloro-4-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(3-ethoxy-phenyl)-pyridin-2-ylamine; (4-{6-amino-5-[1-(2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(3,5-dimethyl-piperazin-1-yl)-methanone; (4-{6-amino-5-[1-(3-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(3,5-dimethyl-piperazin-1-yl)-methanone; 7-[4-(3,5-dimethyl-piperazine-1-carbonyl)-phenyl]-2-phenyl-4H-pyrido[3,2-b][1,4]oxazin-3-one; {4-[6-amino-5-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyridin-3-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone; {4-[6-amino-5-(2,6-difluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone; [4-(6-amino-5-benzyloxy-pyridin-3-yl)-phenyl]-(3,5-dimethyl-piperazin-1-yl)-methanone; (4-{6-amino-5-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-ethyl-piperazin-1-yl)-methanone; [4-(6-amino-5-benzyloxy-pyridin-3-yl)-phenyl]-(4-ethyl-piperazin-1-yl)-methanone; {4-[6-amino-5-(2-methyl-benzyloxy)-pyridin-3-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone; 3-[2-amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl]-benzoic acid methyl ester; 3-[2-amino-5-[4-(3,5-dimethyl-piperazine-1-carbonyl)-phenyl]-pyridin-3-yloxymethyl]-benzoic acid methyl ester; {4-[6-amino-5-(2-methyl-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; [4-(6-amino-5-cyclohexylmethoxy-pyridin-3-yl)-phenyl]-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 4-(1-{2-amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxy}-ethyl)-[2-(3-hydroxy-phenyl)-ethyl]-benzamide; 4-(1-{2-amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxy}-ethyl)-[2-(2,6-dichloro-phenyl)-ethyl]-benzamide; 4-(1-{2-amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxy}-ethyl)-(1-benzyl-piperidin-4-yl)-benzamide; 4-(1-{2-amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxy}-ethyl)-[3-(2-oxo-pyrrolidin-1-yl)-propyl]-benzamide; (4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-ethyl-piperazin-1-yl)-methanone; {4-[6-amino-5-(2,6-dichloro-benzyloxy)-pyridin-3-yl]-phenyl}-(3,5-dimethyl-piperazin-1-yl)-methanone; (6-amino-3-aza-bicyclo[3.1.0]hex-3-yl)-(4-{6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-

ethoxy]-pyridin-3-yl}-phenyl)-methanone; 5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-6'-(2-morpholin-4-yl-ethoxy)-[3,3']bipyridinyl-6-ylamine; 6'-amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-1-(2-pyrrolidin-1-yl-ethyl)-1H-[3,3']bipyridinyl-6-one; 5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-6'-(2-pyrrolidin-1-yl-ethoxy)-[3,3']bipyridinyl-6-ylamine; 6'-amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-1-[2-(1-methyl-pyrrolidin-2-yl)-ethyl]-1H-[3,3']bipyridinyl-6-one; (4-{6-amino-5-[1-(2,4,6-trimethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; (4-{6-amino-5-[1-(2-chloro-6-fluoro-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(4-fluoro-phenyl)-pyridin-2-ylamine; 6'-amino-5'-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-1H-[3,3']bipyridinyl-6-one; 5'-bromo-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-[3,3']bipyridinyl-6-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(4-dimethylamino-phenyl)-pyridin-2-ylamine; 5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-2'-methoxy-[3,3']bipyridinyl-6-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(1H-indol-5-yl)-pyridin-2-ylamine; (4-{6-amino-5-[1-(2,6-dichloro-phenyl)-propoxy]-pyridin-3-yl}-phenyl)-(3,5-dimethyl-piperazin-1-yl)-methanone; [4-(6-amino-5-benzyloxy-pyridin-3-yl)-phenyl]-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 3-(2,6-dichloro-3-fluoro-benzyloxy)-5-thiazol-2-yl-pyridin-2-ylamine; (4-{6-amino-5-[1-(2-fluoro-6-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 3-(2,6-dichloro-3-fluoro-benzyloxy)-5-(1-methyl-1H-imidazol-2-yl)-pyridin-2-ylamine; {4-[6-amino-5-(2,4,6-trimethyl-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {4-[6-amino-5-(2,3,5,6-tetramethyl-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {4-[6-amino-5-(2,4,6-trifluoro-benzyloxy)-pyridin-3-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; (4-{6-amino-5-[1-(2-fluoro-6-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-N-methyl-nicotinamidine; 6-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-N-(2-morpholin-4-yl-ethyl)-nicotinamidine; (4-{6-amino-5-[1-(2,4,5-trifluoro-phenyl)-propoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; (4-{6-amino-5-[1-(6-chloro-2-fluoro-3-methyl-phenyl)-ethoxy]-pyridin-3-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 3-(1-[2-amino-5-[4-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-phenyl]-pyridin-3-yloxy}-ethyl)-benzoic acid; and pharmaceutically acceptable salts, hydrates and solvates thereof.

39. A compound selected from the group consisting of: 3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide; 3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide; 3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; 3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; 3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; N-[2-(4-acetyl-piperazin-1-yl)-ethyl]-3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-benzamide; (3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; (3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; (3-{5-amino-6-[1-(2-chloro-3,6-

167

difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone; (3-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone; 4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-benzoic acid; 4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide; (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone; 4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; 4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; 4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; N-[2-(4-acetyl-piperazin-1-yl)-ethyl]-4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-benzamide; 2-[4-(2-Hydroxy-acetyl)-piperazin-1-yl]-ethanesulfonic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 3-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-benzoic acid; {3-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 3-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-N-{2-[ethyl-(2-methoxy-ethyl)-amino]-ethyl}-benzamide; {3-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; 3-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-N-(3-pyrrolidin-1-yl-propyl)-benzamide; N-[2-(4-acetyl-piperazin-1-yl)-ethyl]-3-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-benzamide; {4-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {4-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone; {4-[5-amino-6-(3-fluoro-2-trifluoromethyl-benzyloxy)-pyrazin-2-yl]-phenyl}-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; 3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; 3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; 3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(3-morpholin-4-yl-propyl)-benzamide; (3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-cyclopropylamino-piperidin-1-yl)-methanone; 3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-((S)-2-hydroxy-3-morpholin-4-yl-propyl)-benzamide; 3-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-((R)-2-hydroxy-3-pyrrolidin-1-yl-propyl)-benzamide; (3-{5-amino-5-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-

pyridin-3-yl)-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 2-diethylamino-ethanesulfonic acid (4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-(4-Hydroxy-piperidin-1-yl)-ethanesulfonic acid (4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-dimethylamino-ethanesulfonic acid (4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-((R)-3-Hydroxy-pyrrolidin-1-yl)-ethanesulfonic acid (4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 2-pyrrolidin-1-ylethanesulfonic acid (4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-benzoic acid; 4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-((R)-2-hydroxy-3-pyrrolidin-1-yl-propyl)-benzamide; (4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-cyclopropylamino-piperidin-1-yl)-methanone; 4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-((S)-2-hydroxy-3-pyrrolidin-1-yl-propyl)-benzamide; 4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-((R)-2-hydroxy-3-morpholin-4-yl-propyl)-benzamide; 4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; (4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; (4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-benzoic acid; (4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; 4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; (4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; (4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; (4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((R)-3-aminopyrrolidin-1-yl)-methanone; (4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-3-aminopyrrolidin-1-yl)-methanone hydrogen chloride; 4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; 4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide; 3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-benzoic acid; 3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(1-methyl-piperidin-4-yl)-benzamide; 3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-pyrrolidin-1-yl-ethyl)-benzamide; (3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; 3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-morpholin-4-yl-ethyl)-benzamide; (3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; (3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-

168

phenyl)-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; N-[2-(4-acetyl-piperazin-1-yl)-ethyl]-4-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-benzamide; N-[2-(4-acetyl-piperazin-1-yl)-ethyl]-3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-benzamide; (3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; 3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(3-pyrrolidin-1-yl-propyl)-benzamide; (3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((S)-3-amino-pyrrolidin-1-yl)-methanone; (3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-((R)-3-amino-pyrrolidin-1-yl)-methanone hydrochloride salt; (3-{5-amino-6-[1-(2,6-dichloro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-(4-methyl-piperazin-1-yl)-methanone; 1-(4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-3-(2-morpholin-4-yl-ethyl)-urea; (R)-2-pyrrolidin-1-ylmethyl-pyrrolidine-1-carboxylic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 1-(4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-3-(2-pyrrolidin-1-yl-ethyl)-urea; 4-methyl-piperazine-1-carboxylic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 1-(4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-3-(2-hydroxy-ethyl)-urea; (S)-3-amino-pyrrolidine-1-carboxylic acid (4-{5-amino-6-[1-(2-chloro-3,6-difluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 1-(4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-3-(1-methyl-piperidin-4-yl)-urea; 4-methyl-piperazine-1-carboxylic acid (4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 1-(4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-3-(2-hydroxy-ethyl)-urea; (S)-3-amino-pyrrolidine-1-carboxylic acid (4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-amide; 1-(4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-phenyl)-3-(1-methyl-piperidin-4-yl)-urea; 5-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophene-2-carboxylic acid; {5-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophen-2-yl}-(4-methyl-piperazin-1-yl)-methanone; {5-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophen-2-yl}-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone; {5-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophen-2-yl}-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-methanone; {5-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophen-2-yl}-((R)-2-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-methanone; 5-[5-amino-6-(2-chloro-3,6-difluoro-benzyloxy)-pyrazin-2-yl]-thiophene-2-carboxylic acid (2-morpholin-4-yl-ethyl)-amide; 3-[1-(2,6-dichloro-3-fluorophenyl)ethoxy]-5-{5-[(4-methylpiperazin-1-yl)carbonyl]pyridin-2-yl}pyrazin-2-amine trifluoroacetate; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-pyridin-4-yl-pyrazin-2-ylamine; 3-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-5-(1H-pyrrol-2-yl)-pyrazin-2-ylamine; (6-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-pyridin-3-yl)-(4-methyl-piperazin-1-yl)-methanone; (2-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-pyridin-4-yl)-(4-methyl-piperazin-1-yl)-methanone; (6-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-pyridin-2-yl)-(4-methyl-piperazin-1-yl)-methanone; (5-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-pyridin-3-yl)-(4-methyl-piperazin-1-yl)-methanone; (4-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-pyridin-2-yl)-(4-methyl-piperazin-1-yl)-methanone; 6-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-morpholin-4-yl-ethyl)-nicotinamide; 5-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(2-morpholin-4-yl-ethyl)-nicotinamide; 6-{5-amino-6-[1-(2,6-

dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(3-morpholin-4-yl-propyl)-nicotinamide; 5-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-N-(3-morpholin-4-yl-propyl)-nicotinamide; (6-{5-amino-6-[1-(2,6-dichloro-3-fluoro-phenyl)-ethoxy]-pyrazin-2-yl}-pyridin-3-yl)-(4-isopropyl-piperazin-1-yl)-methanone; and pharmaceutically acceptable salts, hydrates and solvates thereof.

40. A compound selected from the group consisting the compounds shown in Table 5 and pharmaceutically acceptable salts, hydrates and solvates thereof.

41. A compound selected from the group consisting the compounds shown in Table 6 and pharmaceutically acceptable salts, hydrates and solvates thereof.

42. A compound selected from the group consisting the compounds shown in Table 7 and pharmaceutically acceptable salts, hydrates and solvates thereof.

43. A compound selected from the group consisting the compounds shown in Table 8 and pharmaceutically acceptable salts, hydrates and solvates thereof.

44. A method of treating abnormal cell growth in a mammal, the method comprising administering to the mammal a therapeutically acceptable amount of a compound, salt, hydrate or solvate of any of claims 1-43.

45. The method of claim 44, wherein the abnormal cell growth is cancer.

46. The method of claim 45, wherein the cancer is selected from lung cancer, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, colon cancer, breast cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's Disease, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, prostate cancer, chronic or acute leukemia, lymphocytic lymphomas, cancer of the bladder, cancer of the kidney or ureter, renal cell carcinoma, carcinoma of the renal pelvis, neoplasms of the central nervous system (CNS), primary CNS lymphoma, spinal axis tumors, brain stem glioma, pituitary adenoma, and combinations thereof.

47. The method of 45, wherein the cancer is selected from gastrointestinal stromal tumors, renal cell carcinoma, breast cancer, colorectal cancer, non-small cell lung cancer, neuroendocrine tumors, thyroid cancer, small cell lung cancer, mastocytosis, glioma, sarcoma, acute myeloid leukemia, prostate cancer, lymphoma, and combinations thereof.

169

48. The method of claim 44, wherein the method further comprises co-administering an anti-tumor agent selected from the group consisting of mitotic inhibitors, alkylating agents, anti-metabolites, intercalating antibiotics, growth factor inhibitors, cell cycle inhibitors, enzymes, topoisomerase inhibitors, biological response modifiers, antibodies, cytotoxics, anti-hormones, anti-androgens and mixtures thereof.

120

COMPUESTOS DE AMINOHETEROARILO COMO INHIBIDORES DE LAS PROTEINQUINASAS

CAMPO DEL INVENTO

El presente invento generalmente se relaciona con métodos y compuestos químicos novedosos. Más particularmente, el invento proporciona compuestos novedosos de aminoheteroarilo, particularmente aminopiridinas y aminopirazinas con actividad proteintirosinaquinasa, y métodos para sintetizar y utilizar tales compuestos.

FUNDAMENTO

Las proteinquinasas ("PKs") son enzimas que catalizan la fosforilación de grupos hidroxilos sobre tirosina, residuos de serina y treonina de proteínas. Las consecuencias de esta actividad aparentemente simple son escalonamiento; crecimiento celular, diferenciación y proliferación, es decir, virtualmente todos los aspectos de la vida celular dependen en una u otra forma de la actividad PK. Además, la actividad PK anormal ha sido relacionada con un grupo de trastornos, que van desde enfermedades relativamente moderadas tales como psoriasis hasta enfermedades extremadamente virulentas tales como glioblastoma (cáncer cerebral).

Las PKs pueden ser convenientemente divididas en dos clases, las proteintirosinaquinasas (PTKs) y las serina- treoninaquinasas (STKs).

Uno de los principales aspectos de la actividad PTK es su relación con receptores de factor de crecimiento. Los receptores de factor de crecimiento son proteínas de superficie celular. Cuando están unidos por un ligando de factor de crecimiento, los receptores de factor de crecimiento se convierten en una forma activa la cual interactúa con proteínas sobre la superficie interior de una membrana celular. Esto conduce a la fosforilación sobre residuos de tirosina del receptor y otras proteínas y a la formación dentro de la célula de complejos con una variedad de moléculas de señalización de citoplasma que, a su vez, realizan numerosas respuestas celulares tal como división celular (proliferación), diferenciación celular, crecimiento celular, expresión de efectos metabólicos al microambiente extracelular, etc. para una discusión más completa, ver Schlessinger y Ullrich, Neuron, 9:303- 391 (1992) el cual es incorporado en la presente como referencia, incluyendo cualquier ilustración.

Los receptores de factor de crecimiento con actividad PTK son conocidos como receptores con actividad tirosinaquinasa ("RTKs"). Estos comprenden una gran familia

de receptores de transmembrana con actividad biológica diversa. Actualmente, al menos 19 subfamilias distintas de RTKs han sido identificadas. Por ejemplo entre éstas se encuentra la subfamilia designada "HER" RTKs, la cual incluye EGFR (receptor de factor de crecimiento epitelial), HER2, HER3 y HER4. Estos RTKs constan de un dominio de unión de ligando glicolizado extracelular, un dominio de transmembrana y un dominio catalítico de citoplasma intracelular que puede fosforilar residuos de tirosina sobre proteínas.

Otra subfamilia RTK consta de un receptor de insulina (IR), receptor de factor de crecimiento I tipo insulina (IGF- 1R) y receptor relacionado con receptor de insulina (IRR). IR y IGF- 1R interactúan con insulina, IGF- I y IGF- II para formar un heterotetrámero de dos alfa subunidades glicosiladas totalmente extracelulares y dos beta subunidades las cuales cruzan la membrana celular y contienen el dominio de la tirosinaquinasa.

Una tercera subfamilia RTK es conocida como el grupo de receptores de factor de crecimiento derivado de plaquetas ("PDGFR"), el cual incluye PDGFRalfa, PDGFRbeta, CSFIR, c- kit y c- fms. Estos receptores constan de dominios extracelulares glicosilados compuestos de números variables de bucles tipo inmunoglobulina y un dominio intracelular en donde el dominio de la tirosinatirosina es interrumpido por secuencias aminoácidas no relacionadas.

Otro grupo el cual debido a su similitud con la subfamilia PDGFR, algunas veces es incluido en el último grupo es la subfamilia de receptores de la quinasa de hígado fetal ("flk"). Se cree que este grupo está compuesto de receptor de dominio de inserto de quinasa quinasa- 1 de higado fetal (KDR/FLK- 1, VEGF- R2), flk, 1R, flk- 4, y quinasa 1 de tirosina tipo fms (flt- 1).

Un miembro adicional de la familia de receptores del factor de crecimiento de la tirosinaquinasa es el subgrupo de receptores del factor de crecimiento de fibroblastos ("FGF"). Este grupo consta de cuatro receptores, FGR1- 4, y siete ligandos, FGF1- 7. Mientras no está aún bien definido, parece que los receptores constan de un dominio extracelular glicosilado que contiene un número variable de bucles tipo inmunoglobulina y un dominio intracelular en el cual la secuencia de la tirosinaquinasa es interrumpida por regiones de secuencias aminoácidas no relacionadas.

Aún otro miembro de la familia de receptores del factor de crecimiento de la tirosinaquinasa es el subgrupo de receptores del factor de crecimiento endotelial vascular ("VEGF"). VEFG es una glicoproteína dimérica similar a PDGF pero tiene

diferentes funciones biológicas y especificidad de células objetivo in vivo. En particular, se considera que VEGF juega un papel esencial en vasculogenesis y angiogenesis.

Aún otro miembro de la familia de receptores del factor de crecimiento de la tirosinaquinasa es MET, a menudo conocido como c- Met, también conocido como receptor con actividad tirosinaquinasa de factor de crecimiento de hepatocitos humanos (hHGFR). Se considera que c- Met juega un papel en crecimiento tumoral primario y metastasis.

Un listado más completo de las subfamilias RTK conocidas es descrito en Plowman, DN&P, 7(6):334- 339 (1994) el cual es incorporado en la presente como referencia, incluyendo cualquier ilustración.

Además de las RTKs, también existe una familia de PTKs totalmente intracelulares llamadas "tirosinaquinasas no receptoras") o "tirosinaquinasas celulares". Esta última designación, abreviada "CTK," será utilizada en la presente. Las CTKs no contienen dominios extracelulares y de transmembrana. Actualmente, más de 24 CTKs el 11 subfamilias (Src, Frk, Btk, Csk, Abl, Zap70, Fes, Fps, Fak, Jak y Ack) han sido identificadas. La subfamilia Src parece ser el grupo más grande de CTKs e incluye Src, Yes, Ftn, Lyn, Lck, Blk, HCk, Fgr y Yrk. Para una discusión más detallada de las CTKs, ver Bolen, Oncogene, 8:2025- 2031 (1993), el cual es incorporado en la presente como referencia incluyendo cualquier ilustración.

Las serina/treonina quinasas, STKs, como las CTKs, son predominantemente intracelulares aunque hay muy pocas quinasas receptoras del tipo STK. Las STKs son las más comunes de las quinasas citosólicas; es decir, quinasas que realizan su función en aquella parte del citoplasma diferente a los organelos citoplasmicos y citoesqueleto. El citosol es la región dentro de la célula donde mucha de la actividad metabólica intermediaria y biosintética de la célula ocurre; ejemplo, es en el citosol en donde las proteínas son sintetizadas sobre los ribosomas. Las STKs incluyen CDk2, Raf, la familia de quinasas ZC, la familia de quinasas NEK y BUB1.

Las RTKs, CTKs y STKs todas han sido implicadas en un sinnúmero de condiciones patogénicas incluyendo, significativamente, cáncer. Otras condiciones patogénicas las cuales han sido asociadas con las PTKs incluyen, sin limitación, soriasis, cirrosis hepática, diabetes, angiogenesis, restenosis, enfermedades oftálmicas, artritis reumatoide y otros trastornos inflamatorios, trastornos inmunologicos tales como

enfermedad autoinmune, enfermedad cardiovascular tal como aterosclerosis y una variedad de trastornos renales.

Con respecto al cáncer, dos de las principales hipótesis propuestas para explicar la proliferación celular excesiva que promueve el crecimiento turmoral se relacionan con funciones que se consideran reguladas por PK. Es decir, se ha indicado que el crecimiento celular maligno resulta a partir de un malfuncionamiento de los mecanismos que controlan la división celular y/o diferenciación celular. Se ha mostrado que los productos proteícos de un número de proto- oncógenos están relacionados con las rutas de transducción de señales que regulan la diferenciación y crecimiento celular. Estos productos proteícos de proto- oncógenos incluyen factores de crecimiento extracelular, receptores de factor de crecimiento de transmembrana PTK (RTKs), PTKs (CTKs) y STKs citosólicas, discutidas anteriormente.

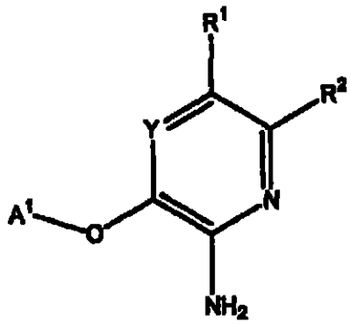
En vista del aparente enlace entre actividades celulares relacionadas con PK y una amplia variedad de trastornos humanos, no es sorprendente que una gran cantidad de esfuerzo sea gastado en un intento por identificar rutas para modular la actividad PK. Una parte de este esfuerzo se ha relacionado con aproximaciones biomiméticas que utilizan moléculas grandes modeladas según aquellas involucradas en los procesos celulares reales (ejemplo, ligandos mutantes (Solicitud US No. 4.966.849); receptores solubles y anticuerpos (Solic. No. WO 94/10202, Kendall y Thomas, Proc. Nat'l Acad. Sci., 90:10705- 09 (1994), Kim, Nature, 362:841- 844 (1993)) ligandos de ARN (Jelinek, Biochemistry, 33:10450- 56); Takano, Mol. Bio. Cell 4:358A (1993); Kinsella, Exp. Cell res. 199:56- 62 (1992); Wright, J. Cellular Phys., 152:448- 57) e inhibidores de la tirosinaquinasa (WO 94/03427; WO 92/21660; WO91/15495; WO 94/14808; Pat. U.S. No. 5.330.992; Mariani, Proc. Am. Assoc. Cancer Res., 35:2268 (1994)).

Además de lo anterior, se han realizado intentos para identificar moléculas pequeñas las cuales actúan como inhibidores PK. Por ejemplo, compuestos de arilo bis-monocíclico, bicíclico y heterocíclico (PCT WO 92/20642), derivados de vinilenazaindol (PCT WO 94/14808) y 1- ciclopropil- 4- piridilquinolonas (U.S. Pat. No. 5.330.992) han sido descritas como inhibidores de la tirosinaquinasa. Compuestos de estirilo (Pat. U.S No. 5.217.999), compuestos de piridilo estirilo- sustituidos (Pat. U.S. No. 5.302.606), derivados de quinazolina (Solicitud EP No. 0 566 266 A1), selenaindoles y seleniuros (PCT WO 94/03427), compuestos tricíclicos polihidroxílicos (PCT WO 92/21660) y compuestos del ácido polihidroxílico (PCT WO 92/21660) y

compuestos del ácido bencilfosfónico (PCT WO 91/15495) todos han sido descritos como inhibidores PTK útiles en el tratamiento del cáncer.

RESUMEN

En una realización, el invento proporciona un compuesto de la formula 1



En donde:

Y es N o CR^{12};

R1 es seleccionado de arilo C6- 12, heterarilo de 5- 12 miembros, cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, - O(CR6R7)nR4, - C(O)R4, - C(O)OR4, - CN, - NO2, - S(O)mR4, - SO2NR4R5, - C(O)NR4R5, - NR4(C(O)R5, - C(=NR6)NR4R5, alquilo C1- 8, alquenilo C2- 8, y alquinilo C2- 8; y cada hidrógeno en R1 es opcionalmente substituido por uno o más grupos R3;

R2 es hidrogeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5, y cada hidrógeno en R2 es opcionalmente sustituido por uno o más grupos R8;

R3 es halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5, cada hidrógeno en R3 es opcionalmente sustituido por uno o más grupos R8, y grupos los R3 sobre átomos adyacentes se pueden combinar para formar un arilo

C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o grupo heteroalicíclico de 3- 12 miembros;

Cada uno de R4, R5, R6 y R7 es independientemente hidrógeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de nitrógeno pueden junto con el nitrógeno al cual están unidos ser combinados para formar un heteroalicíclico de 13 a 12 miembros o grupo heteroarilo de 5- 12 miembros opcionalmente conteniendo de 1 a 3 heteroátomos adicionales seleccionados de N. O y S; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de carbono puede ser combinados para formar un cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, o grupo heteroarilo de 5- 12 miembros; y cada hidrógeno en R4, R5, R6 y R7 es opcionalmente sustituido por uno o más grupos R8;

cada R8 es independientemente halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5 - 12 miembros, - CN, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O- (CH2)n(heteroalicíclico de 3- 12 miembros) o - O- (CH2)n(heteroarilo de 5- 12 miembros); y cada hidrógeno en R8 es opcionalmente sustituido por uno o más grupos R11;

A1 es - (CR9R10)n- A2 excepto que:

(i) cuando Y es N y R1 es arilo sustituido o no sustituido o heteroarilo sustituido o no sustituido, A1 es - (CR9R10)n- A2 y n no es cero; y

(ii) cuando Y es N y R2 es H y A1 es m- clorobencilo, R1 es piperazina no sustituida;

cada R9 y R10 es independientemente hidrógeno, halógeno, alquilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5; R9 y R10 se pueden combinar para formar un cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, arilo C6- 12 o anillo de heteroarilo de 5- 12 miembros; y cada hidrógeno en R9 y R10 es opcionalmente sustituido por uno o más grupos R3;

A2 es arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o heteroalicíclico de 3 - 12 miembros, y A2 es opcionalmente sustituido por uno o más grupos R3;

cada R11 es independientemente halógeno, alquilo C1- 12, alcoxilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5- 12 miembros, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O_(CH2)n(heteroalicíclico de 3- 12 miembros), - O- (CH2)n(heteroarilo de 5- 12 miembros) o - CN, y cada hidrógeno en R11 es un generalmente sustituido por uno o más grupos seleccionados de halógeno - OH, - CN, alquilo C1- 12, el cual puede ser parcial o totalmente halogenado, alquilo - O- C1- 12 el cual puede ser total o parcialmente halogenado, - CO, - SO y - SO2;

R12 es hidrógeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5 y cada hidrogeno en R12 es opcionalmente sustituido por uno o más grupos R3;

R1 y R2 o R1 y R2 se pueden combinar juntos para formar arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12, o grupo heteroalicíclico de 3- 12 miembros;

m es 0, 1 o 2;

n es 0, 1, 2, 3 o 4; y

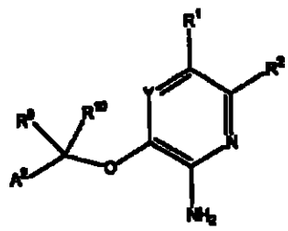
p es 1 o 2;

o una sal, solvato o hidrato farmaceuticamente aceptable del mismo.

En un aspecto particular de esta realización, Y es N. En un aspecto preferido, R1 no es piperazina. En otro aspecto preferido, R1 no es heteroalicíclico.

En otro aspecto particular de esta realización, Y es CR12.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto particular de esta realización, el compuesto tiene la fórmula <u>1a</u>



1a

en donde A2 es arilo C6- 12 o heteroarilo de 5- 12 miembros opcionalmente sustituido por uno o más grupos R3.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto particular de esta realización, R1 es seleccionado de arilo C6- 12 y heteroarilo de 5- 12 miembros, y cada hidrogeno en R1 es opcionalmente sustituido por uno o más grupos R3.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto particular de esta realización consistente con la siguiente definición de R1, R1 es seleccionado de cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, - O(CR8R7)nR4, - C(O)R4, - CN,- - NO2, - S(O)mR4, - SO2NR4R5, - C(O)NR4R5, - C(=NR6)NR4R5, alquilo c1- 8, alquenilo C2- 8, y alquinilo C2- 8; y cada hidrógeno en R1 es opcionalmente substituido por uno o más grupos R3.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto de esta realización, A2 es sustituido por al menos un átomo de halógeno.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto particular de esta realización, R2 es hidrógeno, R9 y R10 son independientemente alquilo C1- 4, y A2 es fenilo sustituido por al menos un átomo de halógeno.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto de esta realización consistente con la siguiente definición de R1, R1 es un furano, tiopeno, pirrola, pirrolina, pirrolidina, dioxolano, oxazol, tiazol, imidazolina, imidazolidina, pirazol, pirazolina, pirazolidina, isoxazol, isotiazol, oxadiazol, triazol, tiadiazol, pirano, piridina, piperidina, dioxano, morfolina, ditiano, tiomorfolina, piridazina, pirimidina, pirazina, piperazina, triazina, tritiano, o grupo fenilo, y cada hidrogeno en R1 es opcionalmente sustituido por uno o más grupos R3.

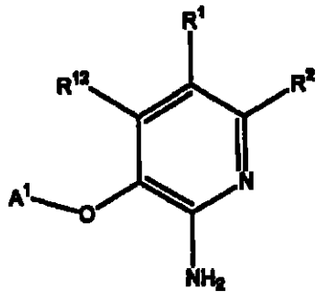
En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto de esta realización consistente con la siguiente definición de R1, R1 es furano, tiopeno, pirrola, pirrolina, pirrolidina, dioxolano, oxazol, tiazol, imidazol, imidazolina, imidazolidina, pirazol, pirazolina, pirazolidina, isoxazol, isotiazol, oxadiazol, tiadiazol, pirano, piridina, piperidina, dioxano, morfolina, ditiano, tiomorfolina, piridazina,

triazina, tritiano, o grupo fenilo, y cada hidrógeno en R1 es opcionalmente sustituido por uno o más grupos R3. En un aspecto más particular, R1 no es heteroalicíclico.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto particular de esta realización consistente con la siguiente definición de R1, R1 es un grupo heteroarilo cíclico fusionado, y cada hidrogeno en R1 es opcionalmente sustituido por uno o más grupos R3.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto particular de esta realización consistente con la siguiente definición de R1, R1 es un grupo - SO_2NR4R5.

En otra realización, el invento proporciona un compuesto de la fórmula 2



2

en donde:

R1 es seleccionado de arilo C6- 12, heterarilo de 5- 12 miembros, cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, - O(CR6R7)nR4, - C(O)R4, - C(O)OR4, - CN, - NO2, - S(O)mR4, - SO2NR4R5, - C(O)NR4R5, - NR4(C(O)R5, - C(=NR6)NR4R5, alquilo C1- 8, alquenilo C2- 8, y alquinilo C2- 8; y cada hidrógeno en R1 es opcionalmente substituido por uno o más grupos R3;

R2 es hidrogeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5, y cada hidrógeno en R2 es opcionalmente sustituido por uno o más grupos R8;

R3 es halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, -

C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5, cada hidrógeno en R3 es opcionalmente sustituido por uno o más grupos R8, y grupos los R3 sobre átomos adyacentes se pueden combinar para formar un arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o grupo heteroalicíclico de 3- 12 miembros;

Cada uno de R4, R5, R6 y R7 es independientemente hidrógeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de nitrógeno pueden junto con el nitrógeno al cual están unidos ser combinados para formar un heteroalicíclico de 13 a 12 miembros o grupo heteroarilo de 5- 12 miembros opcionalmente conteniendo de 1 a 3 heteroátomos adicionales seleccionados de N. O y S; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de carbono puede ser combinados para formar un cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, o grupo heteroarilo de 5- 12 miembros; y cada hidrógeno en R4, R5, R6 y R7 es opcionalmente sustituido por uno o más grupos R8;

cada R8 es independientemente halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5 - 12 miembros, - CN, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O- (CH2)n(heteroalicíclico de 3- 12 miembros) o - O- (CH2)n(heteroarilo de 5- 12 miembros); y cada hidrógeno en R8 es opcionalmente sustituido por uno o más grupos R11;

A1 es - (CR9R10)n- A2 ;

cada R9 y R10 es independientemente hidrógeno, halógeno, alquilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5; R9 y R10 se pueden combinar para formar un cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, arilo C6- 12 o anillo de heteroarilo de 5- 12 miembros; y cada hidrógeno en R9 y R10 es opcionalmente sustituido por uno o más grupos R3;

180

A2 es arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o heteroalicíclico de 3 - 12 miembros, y A2 es opcionalmente sustituido por uno o más grupos R3;

cada R11 es indcpendientemente halógeno, alquilo C1- 12, alcoxilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5- 12 miembros, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O_(CH2)n(heteroalicíclico de 3- 12 miembros), - O- (CH2)n(heteroarilo de 5- 12 miembros) o - CN, y cada hidrógeno en R11 es un generalmente sustituido por uno o más grupos seleccionados de halógeno - OH, - CN, alquilo C1- 12, el cual puede ser parcial o totalmente halogenado, alquilo - O- C1- 12 el cual puede ser total o parcialmente halogenado, - CO, - SO y - SO2;

R12 es hidrógeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5 y cada hidrogeno en R12 es opcionalmente sustituido por uno o más grupos R3;

R1 y R2 o R1 y R2 se pueden combinar juntos para formar arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12, o grupo heteroalicíclico de 3- 12 miembros;

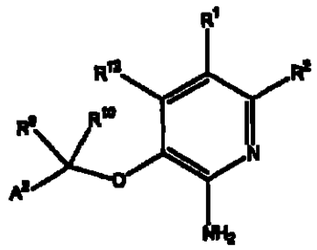
m es 0, 1 o 2;

n es 0, 1, 2, 3 o 4; y

p es 1 o 2;

o una sal, solvato o hidrato farmaceuticamente aceptable del mismo.

En un aspecto particular de esta realización, el compuesto tiene la formula 2a



2a

en donde A2 es arilo C6- 12 o heteroarilo de 5- 12 miembros opcionalmente sustituido por uno o más grupos R3.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto de esta realización, R1 es seleccionado de arilo C1- 12 y heteroarilo de 5- 12 miembros, y cada hidrógeno en R1 es opcionalmente sustituido por uno o más grupos R3.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto de esta realización R1 es seleccionado cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, - O(CR6R7)nR4, - C(O)R4, - C(O)OR4, - CN, - NO2, - S(O)mR4, - SO2NR4R5, - C(O)NR4R5, - NR4(C(O)R5, - C(=NR6)NR4R5, alquilo C1- 8, alquenilo C2- 8, y alquinilo C2- 8; y cada hidrógeno en R1 es opcionalmente substituido por uno o más grupos R3;

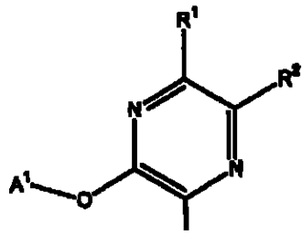
En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto particular de esta realización, R2 es hidrógeno, R9 y R10 son independientemente alquilo C1- 4, A2 es fenilo sustituido por al menos un átomo de halógeno.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto particular de esta realización consistente con la siguiente definición de R1, R1 es furano, tiopeno, pirrola, pirrolina, pirrolidina, dioxolano, oxazol, tiazol, imidazolina, imidazolidina, pirazol, pirazolina, pirazolidina, isoxazol, isotiazol, oxadiazol, triazol, tiadiazol, pirano, piridina, piperidina, dioxano, morfolina, ditiano, tiomorfolina, piridazina, pirimidina, pirazina, piperazina, triazina, tritiano, o grupo fenilo, y cada hidrogeno en R1 es opcionalmente sustituido por uno o más grupos R3.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto particular de esta realización consistente con la siguiente definición de R1, R1 es un grupo heteroarilo cíclico fusionado, y cada hidrógeno en R1 es opcionalmente sustituido por uno o más grupos R3.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto particular de esta realización consistente con la siguiente definición de R1, R1 es un grupo - SO2NR4R5.

En otra realización, el invento proporciona un compuesto la formula 3.



3

en donde:

R1 es seleccionado de arilo C6- 12, heterarilo de 5- 12 miembros, cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, - O(CR6R7)nR4, - C(O)R4, - C(O)OR4, - CN, - NO2, - S(O)mR4, - SO2NR4R5, - C(O)NR4R5, - NR4(C(O)R5, - C(=NR6)NR4R5, alquilo C1- 8, alquenilo C2- 8, y alquinilo C2- 8; y cada hidrógeno en R1 es opcionalmente substituido por uno o más grupos R3;

R2 es hidrogeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5, y cada hidrógeno en R2 es opcionalmente sustituido por uno o más grupos R8;

R3 es halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5, cada hidrógeno en R3 es opcionalmente sustituido por uno o más grupos R8, y grupos los R3 sobre átomos adyacentes se pueden combinar para formar un arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o grupo heteroalicíclico de 3- 12 miembros;

Cada uno de R4, R5, R6 y R7 es independientemente hidrógeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de nitrógeno pueden junto con el nitrógeno al cual están unidos ser combinados para formar un heteroalicíclico de 13 a 12 miembros o grupo heteroarilo de 5- 12 miembros opcionalmente conteniendo de 1 a 3 heteroátomos adicionales seleccionados de N. O y S; o cualquiera dos entre R4, R5, R6

y R7 unidos al mismo átomo de carbono puede ser combinados para formar un cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, o grupo heteroarilo de 5- 12 miembros; y cada hidrógeno en R4, R5, R6 y R7 es opcionalmente sustituido por uno o más grupos R8;

cada R8 es independientemente halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5 - 12 miembros, - CN, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O- (CH2)n(heteroalicíclico de 3- 12 miembros) o - O- (CH2)n(heteroarilo de 5- 12 miembros); y cada hidrógeno en R8 es opcionalmente sustituido por uno o más grupos R11;

A1 es - (CR9R10)n- A2 excepto que:

(i) cuando Y es N y R1 es arilo sustituido o no sustituido o heteroarilo sustituido o no sustituido, A1 es - (CR9R10)n- A2 y n no es cero; y

(ii) cuando Y es N y R2 es H y A1 es m- clorobencilo, R1 es piperazina no sustituida;

cada R9 y R10 es independientemente hidrógeno, halógeno, alquilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5; R9 y R10 se pueden combinar para formar un cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, arilo C6- 12 o anillo de heteroarilo de 5- 12 miembros; y cada hidrógeno en R9 y R10 es opcionalmente sustituido por uno o más grupos R3;

A2 es arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o heteroalicíclico de 3 - 12 miembros, y A2 es opcionalmente sustituido por uno o más grupos R3;

cada R11 es independientemente halógeno, alquilo C1- 12, alcoxilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5- 12 miembros, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O_(CH2)n(heteroalicíclico de 3- 12 miembros), - O- (CH2)n(heteroarilo de 5- 12 miembros) o - CN, y cada hidrógeno en R11 es un generalmente sustituido por uno o más grupos seleccionados de halógeno - OH, - CN, alquilo C1- 12, el cual puede ser parcial o totalmente halogenado, alquilo - O- C1- 12 el cual puede ser total o parcialmente halogenado, - CO, - SO y - SO2;

R1 y R2 se pueden combinar juntos para formar arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12, o grupo heteroalicíclico de 3- 12 miembros;

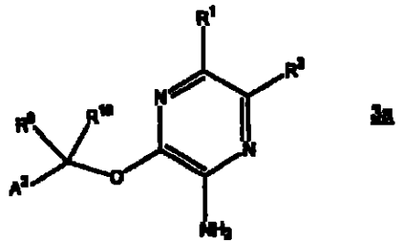
m es 0, 1 o 2;

n es 0, 1, 2, 3 o 4; y

p es 1 o 2;

o una sal, solvato o hidrato farmaceuticamente aceptable del mismo.

En un aspecto particular de esta realización, el compuesto tiene la formula 3a



3a

en donde A2 es arilo C6- 12 o heteroarilo de 5- 12 miembros opcionalmente sustituido con uno más grupos R3.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto particular de esta realización, R1 es seleccionado de arilo C6- 12 y heteroarilo de 5- 12 miembros, y cada hidrogeno en R1 es opcionalmente sustituido por uno o más grupos R3.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto particular de esta realización consistente con la siguiente definición de R1, R1 es seleccionado de cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, - O(CR8R7)nR4, - C(O)R4, - CN,- - NO2, - S(O)mR4, - SO2NR4R5, - C(O)NR4R5, - C(=NR6)NR4R5, alquilo c1- 8, alquenilo C2- 8, y alquinilo C2- 8; y cada hidrógeno en R1 es opcionalmente substituido por uno o más grupos R3.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto de esta realización, A2 es sustituido por al menos un átomo de halógeno.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto particular de esta realización, R2 es hidrógeno, R9 y R10 son independientemente alquilo C1- 4, y A2 es fenilo sustituido por al menos un átomo de halógeno.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto de esta realización consistente con la siguiente definición de R1, R1 es un

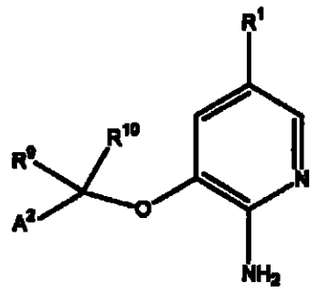
furano, tiopeno, pirrola, pirrolina, pirrolidina, dioxolano, oxazol, tiazol, imidazolina, imidazolidina, pirazol, pirazolina, pirazolidina, isoxazol, isotiazol, oxadiazol, triazol, tiadiazol, pirano, piridina, piperidina, dioxano, morfolina, ditiano, tiomorfolina, piridazina, pirimidina, pirazina, piperazina, triazina, tritiano, o grupo fenilo, y cada hidrogeno en R1 es opcionalmente sustituido por uno o más grupos R3.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto de esta realización consistente con la siguiente definición de R1, R1 es furano, tiopeno, pirrola, pirrolina, pirrolidina, dioxolano, oxazol, tiazol, imidazol, imidazolina, imidazolidina, pirazol, pirazolina, pirazolidina, isoxazol, isotiazol, oxadiazol, tiadiazol, pirano, piridina, piperidina, dioxano, morfolina, ditiano, tiomorfolina, piridazina, triazina, tritiano, o grupo fenilo, y cada hidrógeno en R1 es opcionalmente sustituido por uno o más grupos R3. En un aspecto más particular, R1 no es heteroalicíclico.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto particular de esta realización consistente con la siguiente definición de R1, R1 es un grupo heteroarilo cíclico fusionado, y cada hidrogeno en R1 es opcionalmente sustituido por uno o más grupos R3.

En aspectos particulares de esta realización, y en combinación con cualquier otro aspecto particular de esta realización consistente con la siguiente definición de R1, R1 es un grupo - SO2NR4R5.

En otra realización, el inento proporciona un compuesto de la formula 4



4

en donde:

R1 es seleccionado de arilo C6- 12, heterarilo de 5- 12 miembros, cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, - O(CR6R7)nR4, - C(O)R4, - C(O)OR4, - CN, - NO2, - S(O)mR4, - SO2NR4R5, - C(O)NR4R5, - NR4(C(O)R5, - C(=NR6)NR4R5, alquilo C1- 8, alquenilo C2- 8, y alquinilo C2- 8; y cada hidrógeno en R1 es opcionalmente substituido por uno o más grupos R3;

R3 es halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5, cada hidrógeno en R3 es opcionalmente sustituido por uno o más grupos R8, y grupos los R3 sobre átomos adyacentes se pueden combinar para formar un arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o grupo heteroalicíclico de 3- 12 miembros;

Cada uno de R4, R5, R6 y R7 es independientemente hidrógeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de nitrógeno pueden junto con el nitrógeno al cual están unidos ser combinados para formar un heteroalicíclico de 13 a 12 miembros o grupo heteroarilo de 5- 12 miembros opcionalmente conteniendo de 1 a 3 heteroátomos adicionales seleccionados de N. O y S; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de carbono puede ser combinados para formar un cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, o grupo heteroarilo de 5- 12 miembros; y cada hidrógeno en R4, R5, R6 y R7 es opcionalmente sustituido por uno o más grupos R8;

cada R8 es independientemente halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5 - 12 miembros, - CN, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O- (CH2)n(heteroalicíclico de 3- 12 miembros) o - O- (CH2)n(heteroarilo de 5- 12 miembros); y cada hidrógeno en R8 es opcionalmente sustituido por uno o más grupos R11;

cada R9 y R10 es independientemente hidrógeno, halógeno, alquilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5; R9 y R10 se pueden combinar para formar un cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, arilo C6- 12 o anillo de heteroarilo de 5- 12 miembros; y cada hidrógeno en R9 y R10 es opcionalmente sustituido por uno o más grupos R3;

A2 es arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o heteroalicíclico de 3 - 12 miembros, y A2 es opcionalmente sustituido por uno o más grupos R3;

cada R11 es independientemente halógeno, alquilo C1- 12, alcoxilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5- 12 miembros, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O_(CH2)n(heteroalicíclico de 3- 12 miembros), - O- (CH2)n(heteroarilo de 5- 12 miembros) o - CN, y cada hidrógeno en R11 es un generalmente sustituido por uno o más grupos seleccionados de halógeno - OH, - CN, alquilo C1- 12, el cual puede ser parcial o totalmente halogenado, alquilo - O- C1- 12 el cual puede ser total o parcialmente halogenado, - CO, - SO y - SO2;

m es 0, 1 o 2;

n es 0, 1, 2, 3 o 4; y

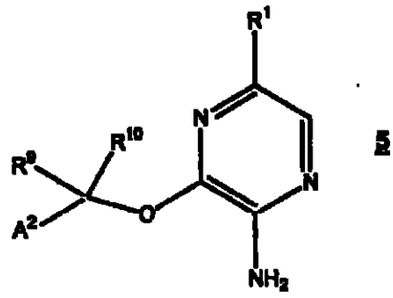
p es 1 o 2;

o una sal, solvato o hidrato farmaceuticamente aceptable del mismo.

En un aspecto particular de esta realización, A2 es arilo C6- 12 o heteroarilo de 5- 12 miembros opcionalmente sustituido por uno o más grupos R3.

En otros aspectos particulares de esta realización, los sustituyentes preferidos y grupos de sustituyentes incluyen aquellos definidos en aspectos particulares de las realizaciones anteriores.

En otra realización, el invento proporciona un compuesto de la formula 5



5

en donde:

R1 es seleccionado de arilo C6- 12, heterarilo de 5- 12 miembros, cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, - O(CR6R7)nR4, - C(O)R4, - C(O)OR4, - CN, - NO2, - S(O)mR4, - SO2NR4R5, - C(O)NR4R5, - NR4(C(O)R5, - C(=NR6)NR4R5, alquilo C1- 8, alquenilo C2- 8, y alquinilo C2- 8; y cada hidrógeno en R1 es opcionalmente substituido por uno o más grupos R3;

R3 es halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5, cada hidrógeno en R3 es opcionalmente sustituido por uno o más grupos R8, y grupos los R3 sobre átomos adyacentes se pueden combinar para formar un arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o grupo heteroalicíclico de 3- 12 miembros;

Cada uno de R4, R5, R6 y R7 es independientemente hidrógeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de nitrógeno pueden junto con el nitrógeno al cual están unidos ser combinados para formar un heteroalicíclico de 13 a 12 miembros o grupo heteroarilo de 5- 12 miembros opcionalmente conteniendo de 1 a 3 heteroátomos adicionales seleccionados de N. O y S; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de carbono puede ser combinados para formar un cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, o grupo heteroarilo de 5- 12 miembros; y cada hidrógeno en R4, R5, R6 y R7 es opcionalmente sustituido por uno o más grupos R8;

cada R8 es independientemente halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5 - 12 miembros, - CN, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O- (CH2)n(heteroalicíclico de 3- 12 miembros) o - O- (CH2)n(heteroarilo de 5- 12 miembros); y cada hidrógeno en R8 es opcionalmente sustituido por uno o más grupos R11;

cada R9 y R10 es independientemente hidrógeno, halógeno, alquilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5; R9 y R10 se pueden combinar para formar un cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, arilo C6- 12 o anillo de heteroarilo de 5- 12 miembros; y cada hidrógeno en R9 y R10 es opcionalmente sustituido por uno o más grupos R3;

A2 es arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o heteroalicíclico de 3 - 12 miembros, y A2 es opcionalmente sustituido por uno o más grupos R3;

cada R11 es independientemente halógeno, alquilo C1- 12, alcoxilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5- 12 miembros, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O_(CH2)n(heteroalicíclico de 3- 12 miembros), - O- (CH2)n(heteroarilo de 5- 12 miembros) o - CN, y cada hidrógeno en R11 es un generalmente sustituido por uno o más grupos seleccionados de halógeno - OH, - CN, alquilo C1- 12, el cual puede ser parcial o totalmente halogenado, alquilo - O- C1- 12 el cual puede ser total o parcialmente halogenado, - CO, - SO y - SO2;

m es 0, 1 o 2;

n es 0, 1, 2, 3 o 4; y

p es 1 o 2;

o una sal, solvato o hidrato farmaceuticamente aceptable del mismo.

En un aspecto particular de esta realización, A2 es arilo C6- 12 o heteroarilo de 5- 12 miembros opcionalmente sustituido por uno o más grupos R3.

En otros aspectos particulares de esta realización, los sustituyentes preferidos y grupos de sustituyentes incluyen aquellos definidos en aspectos particulares de las realizaciones anteriores.

4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenol; 3- (2,6- dicloro- benciloxi)- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- [3- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (1H- indol- 4- il)- piridin- 2- ilamina; 3- [2- cloro- 6- (1H- indol- 4- il)- benciloxi]- 5- (1H- indol- 4- il)- piridin- 2- ilamina; éster tert- butilico del ácido 2- [amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- pirrola- 1- carboxilico; 3- (2,6- dicloro- benciloxi)- 5- (1H- pirrol- 2- il)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (4- fluoro- fenil)- piridin- 2- ilamina;

3- (2,6- dicloro- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (3- fluoro- fenil)- piridin- 2- ilamina; 5- (4- amino- fenil)- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina; N- {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- metanosulfonamida; N- {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- acetamida; 3- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenol; 3-

(2,6- dicloro- benciloxi)- 5- (4- metoxi- fenil)- piridin- 2- ilamina; 5- (3- amino- fenil)- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (3- trifluorometoxi- fenil)- piridin- 2- ilamina; 2- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenol; 3- (2,6- dicloro- benciloxi)- 5- (2- fenoxi- fenil)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (3,4- difluoro- fenil)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (2- isopropil- fenil)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (2- trifluorometil- fenil)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (2- metoxi- fenil)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (4- trifluorometil- fenil)- piridin- 2- ilamina; N- {2- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- metanosulfonamida; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- metanol; 3- (2,6- dicloro- benciloxi)- 5- (2- trifluorometoxi- fenil)- piridin- 2- ilamida; 3- (2,6- dicloro- benciloxi)- 5- (4- metil- tiofen- 2- il)- piridin- 2- ilamida; 5- (2- benciloxi- fenil)- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamida; 3- (2,6- dicloro- benciloxi)- 5- (3- metoxi- fenil)- piridin- 2- ilamida; 3- (2,6- dicloro- benciloxi)- 5- (1H- indol- 2- il)- piridin- 2- ilamida; 5- (4- benciloxi- 3- fluoro- fenil)- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamida; ácido 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- benzoico; 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- N- (2- dietilamino- etil)- benzamida; 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- N- (3- dietilamino- propil)- benzamida; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [4- (2- hidroxi- etil)- piperidin- 1- il)- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(3R)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- ciclopropilaminometil- piperidin- 1- il]- metanona; 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- N- (2- hidroxi- 3- pirrolidin- 1- il- propil)- benzamida; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2(3- fluoro- piperidin- 1- il- ilmetil)- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- (4- ciclopropil- piperazin- 1- il)- metanona;

{4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- [(ciclopropilmetil- amino)- metil]- pirrolidin- 1- il}- metanona; 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- N- [ciclopropilmetil- N- (2R)- pirrolidin- 2- ilmetil- benzamida; 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- N- (2- hidroxi- 3- pirrolidin- 1- il- propil)- N- metil- benzamida; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- {(3R)- 3- hidroxi- pirrolidin- 1- ilmetil]- pirrolidin- 1- il}- metanona; ácido 3- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- benzoico; {3- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il}- metanona; ácido 2{4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenoxi}- acetico; 2- {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenoxi}- 1- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- etanona; 2- {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenoxi}- 1- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- etanona; 3- (2,6- dicloro- benciloxi)- 5- (1H- indol- 5- il)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- [3- (1- metil- 1,2,3,6- tetrahidro- piridin- 4- il)- 1H- indol- 5- il]- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- [3- (1- metil- piperidin- 4- il)- 1H- indol- 5- il]- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (3- morfolin- 4- ilmetil- 1H- indol- 5- il)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (3- piperidin- 1- ilmetil- 1H- indol- 5- il)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (3- pirrolidin- 1- ilmetil- 1H- indol- 5- il)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (3- dietilaminometil- 1H- indol- 5- il)- piridin- 2- ilamina; éster tert- butilico del ácido (1- {5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 3- ilmetil}- (3R)- pirrolidin- 3- il)- carbamico; 3- (2,6- dicloro- benciloxi)- 5- [(2,6- - dimetil- morfolin- 4- ilmetil)- 1H- indol- 5- il]- piridin- 2- ilamina; N- (1- {5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 3- ilmetil}- (3R)- pirrolidin- 3- il)- acetamida; 1- (4{5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 3- ilmetil}- piperazin- 1- il)- etanona; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (1H- indol- 5- il)- piridin- 2- ilamina; 1- (4- {5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- 1H- indol- 3- ilmetil}- piperazin- 1- il)- etanona; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- [3- (2- dimetil- morfolin- 4- ilmetil)- 1H- indol- 5- il]- piridin- 2- ilamina; N- (1- {5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- 1H- indol- 3- ilmetil}- (3S)- pirrolidin- 3- il)- acetamida; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (3- piperidin- 1- ilmetil- 1H- indol- 5- il)- piridin- 2- ilamina; 3- (2- cloro3,6- difluoro- benciloxi)- 5- (3- morfolin- 4- ilmetil- 1H- indol- 5- il]- piridin- 2- ilamina; 3- (2- cloro3,6- difluoro- benciloxi)- 5- (3-

pirrolidin- 1- ilmetil- 1H- indol- 5- il)- piridin- 2- ilamina; éster etilico del ácido 5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carboxilico; ácido 5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carboxilico; {5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- il}- (4- metil- piperazin- 1- il)- metanona; {5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- il}[(3R)- 3- metilamino- pirrolidin- 1- il]- metanona; {5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- il}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; (2- pirrolidin- 1- il- etil)- amida del ácido 5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carboxilico; (2- morfolin- 4- il- etil)- amida del ácido 5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carboxilico; éster tert- butilo del ácido (1- {5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carbonil}- (3S)- pirrolidin- 3- il)- carbamico; (2- hidroxi- 3- pirrolidin- 1- il- propil)- amida del ácido 5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carboxilico; 4(6- amino- 5- benciloxi- piridin- 3- il)- fenol; 3- benciloxi- 5- fenil- piridin- 2- ilamina; 3- (3- metoxi- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2- cloro- 4- fluoro- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2- cloro- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2,5- dicloro- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2- cloro- 5- trifluorometil- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2,4- dicloro- 5- fluoro- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2- cloro- 3- trifluorometil- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (3,4- dicloro- 5- fluoro- benciloxi)- 5- fenil- piridin- 2- ilamina; 2- (2- amino- 5- fenil- piridin- 3- iloximetil)- benzonitrilo; 3- (2- cloro- 6- fluoro- 3- metil- benciloxi)- 5- fenil- piridin- 2- ilamina; 5- fenil- 3- (2,3,6- trifluoro- benciloxi)- piridin- 2- ilamina; 3- (2,6- difluoro- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2,6- difluoro- 3- metil- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (3- cloro- 2,6- difluoro- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2- cloro- 6- fluoro- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (3- fluoro- 4- metoxi- benciloxi)- 5- fenil- piridin- 2- ilamina; N- [3- (2- amino- 5- fenil- piridin- 3- iloximetil)- fenil]- metanosulfonamida; 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- 3- (3- nitro- benciloxi)- piridin- 2- ilamina; 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- 3- (3- naftaleno- 1- ilmetoxi)- piridin- 2- ilamina; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina; 2- {2- amino- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 3- iloxi}- N- (4- isopropil- fenil)- 2- fenil- acetamida; 3- (5- cloro- benzo[b]tiofen- 3- ilmetoxi)- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina; 4- [6- amino- 5- (4- fluoro- 2-

trifluorometil- benciloxi)- piridin- 3- il]- fenil}[(2R)- 2- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- fluoro- 6- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (5- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; (4- {6- amino- 5- [1- (2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- bromo- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; 4- [6- amino- 5- (2- 6- difluoro- benciloxi)- piridin- 3- il]- fenol.; 3- (2,6- difluoro- benciloxi)- 5- (1H- indol- 4- il)- piridin- 2- ilamina; 3- (2,6- difluoro- benciloxi)- 5- [4- (2- morfolin- 4- il- etoxi-)- fenil]- piridin- 2- ilamina, ácido 4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- benzoico, {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; ester etilico del ácido {4- [6- amino- 5- (2,6- fluoro- benciloxi)- piridin- 3- il]- fenoxi- acetico; ácido {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenoxi- acetico; 2- {4- [6- amino- 5- (2,6- fluoro- benciloxi)- piridin- 3- il]- fenoxi}- 1- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- etanona; 2- {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenoxi}- 1- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- etanona; 4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenol; 4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- fenol; 4- [6- amino- 5- (2- 4- dicloro- benciloxi)- piridin- 3- il]- fenol; 2- [2- amino- 5- (4- hidroxi- fenil)- piridin- 3- iloximetil]- benzonitrilo; 4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenol; 4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenol; 4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenol; 4- [6- amino- 5- (4- tert- butilo- benciloxi)- piridin- 3- il]- fenol; N- {4- [6- amino- 5- (2- ciano- benciloxi)- piridin- 3- il]- fenil}metanosulfonamida; 2- [2- amino- 5- (4- metanosulfonilamino- fenil)- piridin- 3- iloximetil]- benzamida; ácido 2- [2- amino- 5- (4- metanosulfonilamino- fenil)- piridin- 3- iloximetil]- benzoico; N- (4- {6- amino- 5- [2- (4- metilpiperazina- 1- carbonil)- benciloxi]- piridin- 3- il}- fenil)- metanosulfonamida; 2- [2- amino- 5- (4- metanosulfonilamino- fenil)- piridin- 3- iloximetil]- N- (2- hidroxi- etil)- benzamida; 2-

[2- amino- 5- (4- metanosulfonilamino- fenil)- piridin- 3- iloximetil]- N- isobutil- benzamida; acido 4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- benzoico; {4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; 1- (4- {4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- benzoil}- piperazin- 1- il)etanona; 4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida; 4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- propil)- benzamida; ácido 4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- benzoico; {4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenil}[(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; {4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; 1- (4- {4[6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- benzoil}- piperazin- 1- il)- etanona; 4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida; 4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- il- propil)- benzamida; ácido 4- [6- amino- 5- (2- ciano- benciloxi)- piridin- 3- il]- benzoico, 2- {2- amino- 5- [4- ((2R)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carbonil)- fenil]- piridin- 3- iloximetil}- benzonitrilo; 2- {2- amino- 5- [4- ((2S)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carbonil)- fenil]- piridin- 3- iloximetil}- benzonitrilo; 2- {2- amino- 5- [4- ((3S)- 3- dimetilamino- pirrolidina- 1- carbonil)- fenil]- piridin- 3- iloximetil}- benzonitrilo; 2- {2- amino- 5- [4- ((3S)- 3- amina- pirrolidina- 1- carbonil)- fenil]- piridin- 3- iloximetil}- benzonitrilo; 2- {2- amino- 5- [4- (4- metil- piperazina- 1- carbonil)- fenil]- piridin- 3- iloximetil}- benzonitrilo; 2- {5- [4- (4- acetil- piperazina- 1- carbonil)- fenil]- 2- amino- piridin- 3- iloximetil}- benzinitrilo; 4- [6- amino- 5- (2- ciano- benciloxi)- piridin- 3- il]- N- (1- metil- piperidin- 4- il)-

benzamida; 4- [6- amino- 5- (2- ciano- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- il-propil)- benzamida; ácido 4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- benzoico; {4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- fenil}[(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; 1- (4- {4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- benzoil}- piperazin- 1- il)- etanona; 4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- N- (1- metil- 1- piperidin- 4- il)- benzamida; 4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- N- (1- morfolin- 4- il- 1- etil)- benzamida; 4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- N- (1- morfolin- 4- il- 1- propil)- benzamida; acido {4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]metanona; {4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]metanona; [(3S)- 3- amino- pirrolidin- 1- il]- {4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- metanona; {4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il]metanona; {4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il]metanona; 1- (4{4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- benzoil}- piperazin- 1- il]etanona; 4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- N- (1- metil- piperidin- 4- il]- benzamida; {4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil]- benzamida; {4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- il- propil]- benzamida; ácido 4- [6- amino- 5- (4- #tert- butilo- benciloxi)- piridin- 3- il]- benzoico; {4- [6- amino- 5- (4- tert- butilo- benciloxi)- piridin- 3- il]fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (4- tert- butilo- benciloxi)- piridin- 3- il]fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (4- tert- butilo- benciloxi)- piridin- 3- il]fenil}- [(3R)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (4- tert- butilo- benciloxi)- piridin- 3- il]fenil}- (4- metil- piperazin- 1- il)- metanona; 1- (4{4- [6- amino- 5- (4- tert- butilo- benciloxi)- piridin- 3- il]- benzoil}- piperazin- 1- il)- etanona; 4- [6- amino- 5- (4- tert- butilo- benciloxi)- piridin- 3- il]- N-

(1- metil- piperidin- 4- il)- benzamida; 4- [6- amino- 5- (4- tert- butilo- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida; 4- [6- amino- 5- (4- tert- butilo- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- il- propil)- benzamida; ácido 4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- benzoico; 4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il]- metanona; 1- (4- {4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- benzoil}- piperazin- 1- il)- etanona; 4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- etil)- benzamida; 4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- propil)- benzamida; ácido 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzoico; {4- [6- amino- 5- (2- cloro- 3,4- difluoro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (4- amino- piperidin- 1- il)- metanona; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il])- metanona; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il])- metanona; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(3R)- 3- amino- 1- pirrolidin- 1- il])- metanona; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il])- metanona; 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (1- metil- piperidin- 4- il])- benzamida; 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (2- pirrolidin- 1- il- etil)- benzamida; 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (3- pirrolidin- 1- propil)- benzamida; 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida; 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- propil-)- benzamida; ácido 3- [6- amino- 5- (2- cloro- 3,6- difluoro-

benciloxi)- piridin- 3- il]- benzoico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il)- metanona; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (4- amino- piperidin- 1- il)- metanona; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(3R)- 3- amino- pirrolidin- 1- il]- metanona; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- amino- pirrolidin- 1- il]- metanona; 3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (1- metil- piperidin- 4- il)- benzamida; 3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (2- pirrolidin- 1- il- etil)- benzamida; 3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (3- pirrolidin- 1- il- propil)- benzamida; 3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida; 3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- propil)- benzamida; N- [2- (4- acetil- piperazin- 1- il)- etil]- 3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzamida; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- [4- (1,1- dioxo- 1λ^6- isotiazolidin- 2- il)- fenil]- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- [4- (1,1- dioxo- 1λ^6- isotiazolidin- 2- il)- fenil]- piridin- 2- ilamina; 5- [4- (1,1- dioxo- 1λ^6- isotiazolidin- 2- il)- fenil]- 3- (2- fluoro- 6- trifluorometil- benciloxi)- piridin- 2- ilamina; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- dietilamino- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- ciclopropilamino- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- pirrolidin- 1- il- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- morfolin- 4- il- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- piperidin- 1- il- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)-

piridin- 3- il]- fenil}- amida del ácido 2- dietilamino- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- (4- acetil- piperazin- 1- il)- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- (ciclopropilmetil- amino)- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- [(3R)- 3- hidroxi- pirrolidin- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- [(2S)- 2- hidroximetil- pirrolidin- 1- il]- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- 4- (2- hidroxi- acetil)- piperazin- 1- il]- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- (4- acetil- piperazin- 1- il)- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- pirrolidin- 1- il- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- morfolin- 4- il- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- dietilamino- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- dimetilamino- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- piperidin- 1- iletanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- [(3R)- 3- hidroximetil- pirrolidin- 1- il]- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- [4- hidroxi- acetil)- piperazin- 1]- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- [(3R)- 3- hidroxi- pirrolidin- 1- il]- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- (ciclopropilmetil- amino)- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- ciclopropilano- etanosulfónico; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (2- dimetilaminometil- fenil)- piridin- 2- ilamina; compuesto con ácido trifluoro- acetico; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (3- pirrolidin- 1- il- fenil)- piridin- 2- ilamina; compuesto con ácido trifluoro- acetico; N- {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- metanosulfonamida; compuesto con ácido trifluoro- acetico; ácido {5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]-

tiofeno- 2- carboxilico; {5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofen- 2- il}- (4- metil- piperazin- 1-)- metanona; {5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofen- 2- il}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; (1- metil- piperidin- 4- il)- amida del ácido 5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofeno- 2- carboxilico; {5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofen- 2- il}- (3,5- metil- piperazin- 1- il)- metanona; (2- pirrolidin- 1- il- etil)- amida del ácido 5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofeno- 2- carboxilico; {5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofen- 2- il}- (4- pirrolidin- 1- il-)- metanona; ácido 4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- benzoico; {4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin –1- piperidin- 1- il)- metanona; 4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- N- (1- metil- piperidin- 4- il)- benzamida; {4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona; {4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (3- dimetilamino- pirrolidin- 1- il)- metanona; {4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; 4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida; {4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; N- [2- (4- acetil- piperazin- 1- il)- etil]- 4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- benzamida; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- piperidin- 1- il- etanosulfónico; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- dimetilamino- etanosulfónico; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- ciclopropilamino- etanosulfónico; ácido 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- benzoico; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- [(2R)- 2- pirrolidin- 1- il)- metanona; 4- {6- amino- 5[1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (1- metil- piperidin- 4- il)- benzamida; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- [(3R)- 3- amino- pirrolidin- 1- il]- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)-

etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperázin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (3,5- dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- cloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- ciclopropilamino- etanosulfónico; (4- {6- amino- 5- [1- (2,6- cloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- dimetilamino- etanosulfónico; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- [(3R)- 3- hidroxi- pirrolidin- 1- il)]- etanosulfónico; y sales, hidratos y solvatos farmacéuticamente aceptables de los mismos.

En otra realización, el invento proporciona un compuesto seleccionado del grupo que consta de 4- [5- amino- 6- (2,6- dicloro- benciloxi)- pirazin- 2- il]- fenol; 3- (2,6- dicloro- benciloxi)- 5- [4- (1,1- dioxo- 1λ^6- isotiazolin- 2- il)- fenil]- pirazin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- [3- (2- morfolin- 4- il- etoxi)- fenil]- pirazin- 2- ilamina; 5- (4- amino- fenil)- 3- (2,6- dicloro- benciloxi)- pirazin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- [3- (2- morfolin- 4- il- etoxi)- fenil]- pirazin- 2- ilamina; ácido 5- [4- amino- 6- (2,6- dicloro- benciloxi)- pirazin- 2- il]- benzoico; {4- [5- amino- 6- (2,6- dicloro- benciloxi)- pirazin- 2- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; 4- [5- amino- 6- (2,6- dicloro- benciloxi)- pirazin- 2- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- morfolin- 4- il- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- piperidin- 1- il- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- pirrolidin- 1- il- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- [(3R)- 3- hidroxi- pirrolidin- 1- il]- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- [(2S)- 2- hidroximetil- pirrolidin- 1- il]- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- (ciclopropilmetil- amino)- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- dimetilamino- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- dietilamino- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)-

pirazin- 2- il]- fenil}- amida del ácido 2- (4- acetil- piperazin- 1- il)- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- [4- (2- hidroxi- acetil)- piperazin- 1- il]- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- ciclopropilamino- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- [(3R)- 3- hidroximetil- pirrolidin- 1- il]- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- (4- acetil- piperazin- 1- il)- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- piperidin- 1- il- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- dietilamino- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- morfolin- 4- il- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- pirrolidin- 1- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- dimetilsmino- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- [4- (2- hidroxi- acetil)- piperazin- 1- il]- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- (ciclopropilmetil- amino)- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- [(3R)- 3- hidroxi- pirrolidin- 1- il]- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- ciclopropilamino- etanosulfónico; ácido 4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- benzoico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; 4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (2- pirrolidin- 1- il- etil)- benzamida; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il]- metanona; N- [2- (4- acetil- piperazin- 1- il)- etil]- 4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- benzamida; 4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (3- pirrolidin- 1- il- propil)- benzamida; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3R)- 3-

dimetilamino- pirrolidin- 1- il]- metanona; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (3- morfolin- 4- il- propil)- benzamida; 4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (1- metil- piperidin- 4- il)- benzamida; 4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (2- morfolin- 4- il- etil)- benzamida; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; ácido 3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- benzoico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3R)- 3- amino- pirrolidin- 1- il]- metanona; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il]- metanona; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3,5- dimetil- piperazin- 1- il)- metanona; 3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (3- morfolin- 4- il- propil)- benzamida; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona; 3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (2- pirrolidin- 1- il- etil)- benzamida; 3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (1- metil- piperidin- 4- il)- benzamida; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(2S)- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; 3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (2- morfolin- 4- etil)- benzamida; N- [2- (4- acetil- piperazin- 1- il)- etil]- 3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- benzamida; 3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (3- pirrolidin- 1- il- propil)- benzamida; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (1H- indol- 5- il)- pirazin- 2- ilamina; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (3- pirrolidin- 1- ilmetil- 1H- indol- 5- il)- pirazin- 2- ilamina; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (3- dietilaminometil- 1H- indol- 5- il)- pirazin- 2- ilamina; 1- (4- {5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- 1H- indol- 3- ilmetil}- piperazin- 1- il)- etanona; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- [3- (2,6- dietil- morfolin- 4- ilmetil)- 1H- indol- 5- il]- pirazin- 2- ilamina; N- (1- {5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin-

2- il]- 1H- indol- 3- ilmetil}(3S)- pirrolidin- 3- il)- acetamida; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (3- piperidin- 1- ilmetil- 1H- indol- 5- il)- pirazin- 2- ilamina; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (3- morfolin- 4- ilmetil- 1H- indol- 5- il)- pirazin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi)- fenil]- pirazin- 2- ilamina; compuesto con ácido trifluoro- acetico; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- pirazin- 2- ilamina; compuesto con ácido trifluoro- acetico; N- (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- metanosulfonamida; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il]- fenil}- amida del ácido 2- pirrolidin- 1- il- etanosulfónico; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido 2- piperidin- 1- il- etanosulfónico; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido 2- (ciclopropilmetil- amino)- etanosulfónico; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido 2- [(3R)- 3- hidroxi- pirrolidin- 1- il]- etanosulfónico; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido 2- dimetilamino- etanosulfónico; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido 2- morfolin- 4- il- etanosulfónico; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido 2- dietilamino- etanosulfónico; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido 2- ciclopropilamino- etanosulfónico; ácido 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- benzoico; (3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}fenil)- [(3S)- 3- amino- pirrolidin- 1- il)- m- etanona; (3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}fenil)- [(3r)- 3- amino- pirrolidin- 1- il)- m- etanona; (3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]pirazin- 2- il}fenil)- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; N- [2- (4- acetil- piperazin- 1- il)- etil]- 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- benzamida; (3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}fenil)- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; ácido 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- benzoico; 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4- il)- benzamida; 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- pirrolidin- 1- il- propil)-

benzamida; (3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il} fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; ácido 4[5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- benzoico; 4- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- N- (1- metil- piperidin- 4- il)- benzamida; y sales, hidratos y solvatos farmacéuticamente aceptables de los mismos.

En otra realización, el invento proporciona un compuesto seleccionado del grupo que consta de (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; N- [2- (4- acetil- piperazin- 1- il)- etil]- 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- benzamida; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((s)- 3- amino- pirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- amino- piperidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 3- hidroxi- pirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 3- hidroxi- pirrolidin- 1- il)- metanona; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 2- hidroximetil- pirrolidin- 1- il)- metanona; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- dietilamino- etil)- benzamida; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; ácido 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- benzoico; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il} fenil)- (4- metil- piperazin- 1- il)- metanona; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (1- metil- piperidin- 4- il)- benzamida; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; N- [2- (4- acetil- piperazin- 1- il)- etil]- 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 3- il}- benzamida; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 3- amino- pirrolidin- 1- il)- metanona; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (3- morfolin- 4- il- propil)- benzamida; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 2-

pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- piperidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- dietilamino- etanosulfónico; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- (ciclopropilmetil- amino)- etanosulfónico; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- ((R)- 3- hidroxi- pirrolidin- 1- il)- etanosulfónico; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- ciclopropilamino- etanosulfónico; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- dietilamino- etanosulfónico;

Ácido 4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- benzoico; 4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida; 4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (1- metil- piperidin- 4- il)- benzamida; (4- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; 4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; (4- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; (4- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 3- amino- pirrolidin- 1- il)- metanona; ácido 3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin-

3- il}- benzoico; (3- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; (3- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona; 3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (1- metil- piperidin- 4- il)- benzamida; (3- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; 3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; 3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; (3- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 3- amino- pirrolidin- 1- il)- metanona; 3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida; (3- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (3- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- [3- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [4- (2- morfolin- 1- il- etoxi)- fenil]- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- {4- [2- (1- metil- pirrolidin- 2- il)- etoxi]- fenil}- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [3- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina; 1- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenoxi)- 3- morfolin- 4- il- propan- 2- ol; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [4- (1- metil- piperidin- 3- ilmetoxi)- fenil]- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [4- (1- metil- piperidin- 4- iloxi)- fenil]- piridin- 2- ilamina; N- (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- metanosulfonamida; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- [1,1- dioxo- 1 lamba*6*- isotiazolidin- 2- il)- fenil]- piridin- 2- ilamina; N- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- metanosulfonamida; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- fenil]- piridin- 2- ilamina; N- (4- {6- amino- 5- [(R)- 1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- metanosulfonamida; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- tiofen- 3- il- piridin- 2- ilamina; 5- benzo[b]tiofen- 2- il- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina;

(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 4- metil- piperazina- 1- carboxilico; 1- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (2- pirrolidin- 1- il- etil)- urea; 1- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (2- hidroxi- etil)- urea; 1- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (2- morfolin- 4- il- etil)- urea; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido (R)- 3- amino- pirrolidina- 1- carboxilico; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido (S)- 3- amino- pirrolidina- 1- carboxilico; 1- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (1- metil- piperidin- 4- il)- urea; 1- (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (1- metil- piperidin- 4- il)- urea; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido (R)- 3- amino- pirrolidina- 1- carboxilico; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido (S)- 3- amino- pirrolidina- 1- carboxilico; 1- (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (2- hidroxi- etil)- urea; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 4- metil- piperazina- 1- carboxilico; 1- (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (2- pirrolidin- 1- il- etil)- urea; 1- (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (2- morfolin- 4- il- etil)- urea; (4- {6- amino- 5- [1- (2- cloro- 3,6- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido (R)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxilico; ácido 3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- benzoico; (3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; (3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; 3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida; (3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; 3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; N- [2- (4- acetil- piperazin- 1- il)- etil]- 3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida; 3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (1- metil- piperidin- 4- il)- benzamida;

(3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; (3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 3- amino- pirrolidin- 1- il)- metanona; (3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona; ácido 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- benzoico; 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida; (4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 2- pirrolidin- 1- il)- metanona; ácido 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- benzoico; 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida; (4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (1- metil- piperidin- 4- il)- benzamida; (4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; N- [2- (4- acetil- piperazin- 1- il)- etil]- 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- benzamida; 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; (4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 3- aminopirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- (R)- 3- amino- pirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- amida del ácido (S)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxilico; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- amida del ácido 4- metil- piperazin- 1- carboxilico; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- amida del ácido 4- pirrolidin- 1- il- piperidina- 1- carboxilico; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- amida del ácido (3R, 5S)- 3,5-

dimetil- piperazina- 1- carboxilico; 1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 3- (1- metil- piperidin- 4- il)- urea; 1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 3- (3- pirrolidin- 1- il- propil)- urea; 1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 3- (2- pirrolidin- 1- il- etil)- urea; 1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 3- (2- morfolin- piperidin- 4- il- etil)- urea; 1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 3- (3- morfolin- 4- il- propil)- urea; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- amida del ácido (R)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxilico;3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3- dimetilamino- prop- 1- inil)- piridin- 2- ilamina; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- urea; N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- piperidin- 1- il- acetamida; N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- morfolin- 4- il- acetamida; N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- pirrolidin- 1- il- acetamida; N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- ((R)- 3- hidroxi- pirrolidin- 1- il)- acetamida; N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- (4- hidroxi- piperidin- 1- il)- acetamida; N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- dimetilamino- acetamida; N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- dietilamino- acetamida; 2- (4- acetil- piperazin- 1- il)- N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- acetamida; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- amida del ácido 4- metil- piperazin- 1- carboxilico; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- amida del ácido (3R, 5S)- 3,5- dimetil- piperazin- 1- carboxilico; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- amida del ácido (3R, 5S)- 3,5- dimetil- piperazin- 1- carboxilico; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- amida del ácido (R)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxilico; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- amida del ácido (S)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxilico; 1- (3- {6- amino- 5- [1- (2,6- dicloro-

3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- 3- (2- morfolin- 4- il-propil)- urea; 1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- 3- (2- pirrolidin- 1- il- etil)- urea; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- amida del ácido 4- pirrolidin- 1- il- piperidina- carboxilico; ciclohexilamida del ácido 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- propinoico; isopropilamida del ácido 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- propinoico; 4- (3- amino- 3- metil- but- 1- inil)- 2- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- fenilamida; (4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- il)- metanona; (4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; 4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- N- (1- metil- piperidin- 4- il)- benzamida; 4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- etil)- benzamida; 4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida; 4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; 4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- N- (3- morfolin- 4- il- propil)- benzamida; 6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- nicotinonitrile; 6- amino- 5- [1- (2,6- dicloro- 3- ciano- fenil)- etoxi]- nicotinonitrile; 5- aminometil- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- ilmetil}- amida del ácido (R)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxilico; N- {6- amino- 5- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- ilmetil}- metanosulfonamida; N- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- ilmetil}- acetamida; N- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- ilmetil}- 4- metil- bencenosulfonamida; 5- aminometil- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- vinil- piridin- 2- ilamina; (S)- 1- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}etano- 1,2- diol; (R)- 1- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}etano- 1,2- diol;

++3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (1H- pirazol- 4- il)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [1- (2- pirrolidin- 1- il- etil)- 1H- pirazol- 4- il]- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [1- (2- diisopropilamino- etil)- 1H- pirazol- 4- il]- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [1- (2- morfolin- 4- il- etil)- 1H- pirazol- 4- il]- piridin- 2- ilamina; 5- bromo- 3- (3- fluoro- 2- metoxi- benciloxi)- piridin- 2- ilamina; 5- bromo- 3- [1- (3- fluoro- 2- metoxi- fenil)- etoxi]- piridin- 2- ilamina; {4- [6- amino- 5- (3- fluoro- 2- metoxi- benciloxi)- piridin- 3- il]- fenil}- ((3R,5S)- 3,5- dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (3- fluoro- 2- metoxi- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R,5S)- 3,5- dimetil- piperazin- 1- il)- metanona; 5- bromo- 3- (3- fluoro- 2- isopropoxi- benciloxi)- piridin- 2- ilamina; {4- [6- amino- 5- (3- fluoro- 2- isopropoxi- benciloxi)- piridin- 3- il]- fenil}- ((3R,5S)- 3,5- dimetil- piperazin- 1- il)- metanona; 5- (4- amino- fenil)- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina; ester metilo del ácido (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenoxi)- acetico; 2- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenoxi)- 1- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- etanona; 2- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenoxi)- 1- ((R)- 3- hidroxi- pirrolidin- 1- il)- etanona; ester tert- butilo del ácido 4- [2- (4- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenoxi)- acetil]- piperazina- 1- carboxilico; 2- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenoxi)- 1- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- etanona; 5- bromo- 3- (3- fluoro- 6,7,8,9- tetrahidro- 5H- benzocicloheptен- 5- iloxi)- piridin- 2- ilamina; {4- [6- amino- 5- (3- fluoro- 6,7,8,9- tetrahidro- 5H- benzocicloheptен- 5- iloxi)- piridin- 3- il]- fenil}- ((3R,5S)- 3,5- dimetil- piperazin- 1- il)- metanona; 3- (3- fluoro- 6,7,8,9- tetrahidro- 5H- benzocicloheptен- 5- iloxi)- 5- [4- (2- pirrolidin- 1- il- etoxi)- fenil]- piridin- 2- ilamina; N- {4- [6- amino- 5- (3- fluoro- 6,7,8,9- tetrahidro- 5H- benzocicloheptен- 5- iloxi)- piridin- 3- il]- fenil}metanosulfonamida; 3- (3- fluoro- 6,7,8,9- tetrahidro- 5H- benzocicloheptен- 5- iloxi)- 5- (1H- pirazol- 4- il)- piridin- 2- ilamina; 5- bromo- 3- [1- (2- cloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina; 3- [1- (2- cloro- 3- fluoro- fenil)- etoxi]- 5- [4- (2- pirrolidin- 1- il- etoxi-)- fenil]- piridin- 2- ilamina; 5`- benciloxi- [2,3]bipiridinil- 6`- ilamina; 5- benciloxi- [3,3`]bipiridinil- 6- ilamina; 3- benciloxi- 5- pirimidin- 5- il- piridin- 2- ilamina; 5`- benciloxi- [2,3]bipiridinil- 6`- ilamina; 5- benciloxi- [3,3`]bipiridinil- 6,6`- ilamina;diamina; 5- (2- cloro- benciloxi)- [2,3`]bipiridinil- 6`-

ilamina; 5- (2- cloro- benciloxi)- [3,3`]bipiridinil- 6- ilamina; 3- (2- cloro- benciloxi)- 5- oirimidin- 5- il- piridin- 2- ilamia; 5- (2- cloro- benciloxi)- [3,3`]bipiridinil- 6,6′- diamina; 5′- (4- cloro- benciloxi)- [2,3`]bipiridinil- 6′- ilamina; 5- (4- cloro- benciloxi)- [3,3`]bipiridinil- 6- ilamina; 3- (4- cloro- benciloxi)- 5- pirimidin- 5- il- piridin- 2- ilamina; 5- (4- cloro- benciloxi)- [3,3`]bipiridinil- 6,6′- diamina; 5′- (2- cloro- 3,6- difluoro- benciloxi)- [2,3`]bipiridinil- 6′- ilamina; 5′- (2- cloro- 3,6- difluoro- benciloxi)- [3,3`]bipiridinil- 6- ilamina; 5- (2- cloro- 3,6- difluoro- benciloxi)- [2,4`]bipiridinil- 6′- ilamina; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- pirimidin- 5- il- piridin- 2- ilamia; 5- (2- cloro- 3,6- difluoro- benciloxi)- [3,3`]bipiridinil- 6,6′- diamina; 5′- (2,6- dicloro- benciloxi)- [2,3`]bipiridinil- 6′- ilamina; 5′- (2,6- dicloro- benciloxi)- [3,3`]bipiridinil- 6- ilamina; 5- (2,6- dicloro- benciloxi)- [3,4`]bipiridinil- 6′- ilamina; 3- (2,6- dicloro- benciloxi)- 5- pirimidin- 5- il- piridin- 2- ilamina; 5- (2,6- dicloro- benciloxi)- [3,3`]bipiridinil- 6,6′- diamina; 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [3,3`]bipiridinil- 6,6′- diamina; {6′- amino- 5′- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [2,3′]bipiridin- 4- il}- (4- metil- piperazin- 1- il)- metanona; {6′- amino- 5′- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [2,3′]bipiridin- 6- il}- (4- metil- piperazin- 1- il)- metanona; {6′- amino- 5′- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [3,3′]bipiridin- 5- il}- (4- metil- piperazin- 1- il)- metanona; {6′- amino- 5′- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [3,3′]bipiridin- 6- il}- (4- metil- piperazin- 1- il)- metanona; {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [3,4′]bipiridin- 2′- il}- (4- metil- piperazin- 1- il)- metanona; 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [3,3`]bipiridinil- 6,6′- diamina; {6′- amino- 5′- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [2,3′]bipiridin- 5- il}- (4- metil- piperazin- 1- il)- metanona; {6′- amino- 5′- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [2,3′]bipiridin- 4- il}- (4- metil- piperazin- 1- il)- metanona; {6′- amino- 5′- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [2,3′]bipiridin- 6- il}- (4- metil- piperazin- 1- il)- metanona; {6′- amino- 5′- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [3,3′]bipiridin- 5- il}- (4- metil- piperazin- 1- il)- metanona; {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [3,4′]bipiridin- 2′- il}- (4- metil- piperazin- 1- il)- metanona; 5′- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [2,3′]bipiridin- 6′- ilamina; 5′- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [2,3′]bipiridin- 6′- ilamina; 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [3,3′]bipiridin- 6- ilamina; 5′- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- pirimidin- 5- il- piridin- 2- ilamina; {6′- amino- 5′- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [2,3′]bipiridin- 5- il}- (4- metil- piperazin- 1- il)- metanona; 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [3,4′]bipiridin- 6- ilamina; 5- benciloxi- 3- [1- (2-

cloro- 3,6- difluoro- fenil)- etoxi]- [3,3']bipiridin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- (2- etil- butoxi)- piridin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- (3- metil- butoxi)- piridin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- butoxi- piridin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- propoxi- piridin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- ciclohexilmetoxi- piridin- 2- ilamina; 6- amino- 5- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- piridin- 3- ol; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- (2- ciclohexil- etoxi)- piridin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- isobutoxi- piridin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- fenetiloxi- piridin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- (piridin- 4- ilmetoxi)- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 2- fluoro- benzonitrilo; 4- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- piperidin- 4- ol; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- piperidin- 1- il- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- pirrolidin- 1- il- metanona; ester metilo del ácido (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- metil- benzoico; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [4- (dimetil- piperazin- 1- ilmetil)- fenil]- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 3,5- dimetoxi- fenil)- (dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 2- fluoro- fenil)- (dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 3- fluoro- fenil)- (dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 3- metil- fenil)- (dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- [1,4]diazepan- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- [1,4]diazepan- 1- il- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- piperazin- 1- il- metanona; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- vinil- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R)- 3,4- dihidroxi- pirrolidin- 1- il)- metanona; 5- [(1- bencil- pirrolidin- 3- ilamino)- metil]-

3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- azetidin- 3- il- benzamida; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N,N- dimetil- bencenosulfonamida; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (6- metoxi- 1H- benzoimidazol- 2- il)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (6- metoxi- 1- metil- 1H- benzoimidazol- 2- il)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [4- (4- metil- [1,4]diazepano- 1- sulfonil)- fenil]- piridin- 2- ilamina; amida del ácido 6{6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1- metil- 1H- indazol- 3- carboxilico; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (1- metil- 1H- pirazol- 4- il)- piridin- 2- ilamina; 5- (3- cloro- fenil)- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (4- fluoro- 3- metil- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3- trifluorometil- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3- trifluorometoxi- fenil)- piridin- 2- ilamina; 5- benzo[1,3]dioxol- 5- il- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina; 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenol; 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- metanol; 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- benzonitrilo; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3- metoxi- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3,5- dicloro- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,5- dimetil- fenil)- piridin- 2- ilamina; 5- (5- cloro- 2- metoxi- fenil)- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,5- dimetil- fenil)- piridin- 2- ilamina; 5- (3- cloro- 4- fluoro- fenil)- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,5- dimetil- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (5- fluoro- 2- metoxi- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3- isopropil- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3,4- dicloro- fenil)- piridin- 2- ilamina; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- benzonitrilo; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3,4- difluoro- fenil)- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((2R,6S)- 2,6- dimetilmorfolin- 4- il)- metanona; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2- etoxi- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (5,2- dimetoxi- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,4- dimetoxi- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3-

fluoro- fenil)- etoxi]- 5- (2- trifluorometil- fenil)- piridin- 2- ilamina; 5- (2- cloro- fenil)- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,5- dimetil- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2- trifluorometoxi- fenil)- piridin- 2- ilamina; 1- (2- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- etanona; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2- fluoro- fenil)- piridin- 2- ilamina; (2- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- metanol; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- o- tolil- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2- metoxi- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,6- dimetil- fenil)- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- morfolin- 4- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 2- cloro- fenil- ((3R,5S)- dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 2- metil- fenil)- ((3R,5S)- dimetil- piperazin- 1- il)- metanona; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [4- ((2R, 6S)- 2,6- dimetil- morfolin- 4- ilmetil)- fenil]- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (4- morfolin- 4- ilmetil- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3,5- dimetil- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- m- tolil- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3,4- dimetoxi- fenil)- piridin- 2- ilamina; 5- bifenil- il- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina; 5- (3,5- bis- trifluorometil- fenil)- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- 5- (3,4- dicloro- fenil)- piridin- 2- ilamina; 1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- etona; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3,5- difluoro- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,5- dicloro- fenil)- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2,6- dicloro- 4- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3- etoxi- fenil)- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- (3,5- dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (3- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- (3,5- dimetil- piperazin- 1- il)- metanona; 7- [4- (3,5- dimetil- piperazin- 1- carbonil)- fenil]- 2- femil- 4H- pirido[3,2- b]pxazin- 3- ona; (4- {6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]etoxi]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona; {4- {6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenil}-

(3,5- dimetil- piperazin- 1- il)- metanona; [4- {6- amino- 5- benciloxi- piridin- 3- il)- fenil]- (3,5- dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2- clor- 3,6- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- etil- piperazin- 1- il)- metanona; [4- {6- amino- 5- benciloxi- piridin- 3- il)- fenil]- (4- etil- piperazin- 1- il)- metanona; {4- [6- amino- 5- (2- metil- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona; ester metilico del ácido 3- {2- amino- 5- [4- (4- pirrolidin- 1- piperidina- 1- carbonil)- fenil]- piridin- 3- iloximetil}benzoico; ester metilico del ácido 3- {2- amino- 5- [4- (3,5- dimetil- piperazina- 1- carbonil)- fenil]- piridin- 3- iloximetil}benzoico; {4- [6- amino- 5- (2- metil- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; [4- (6- amino- 5- ciclohexilmetoxi- piridin- 3- il)- fenil]- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 4- (1- {2- amino- 5- [4- (4- pirrolidin- 1- il- piperidina- 1- il- carbonil)- fenil]- piridin- 3- iloxi}- etil)- [2- (3- hidroxi- fenil)- etil]- benzamida; 4- (1- {2- amino- 5- [4- (4- pirrolidin- 1- il- piperidina- 1- il- carbonil)- fenil]- piridin- 3- iloxi}- etil)- [2- (2,6dicloro- fenil)- etil]- benzamida; 4- (1- {2- amino- 5- [4- (4- pirrolidin- 1- il- piperidina- 1- il- carbonil)- fenil]- piridin- 3- iloxi}- etil)- (1- bencil- piperidin- 4- il)- benzamida; 4- (1- {2- amino- 5- [4- (4- pirrolidin- 1- il- piperidina- 1- il- carbonil)- fenil]- piridin- 3- iloxi}- etil)- [3- (2- oxo- pirrolidin- 1- il)- propil]- benzamida; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- etil- piperazin- 1- il)- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona; (6- amino- 3- aza- biciclo[3.1.0]hex- 3- il)- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- metanona; 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 6'- (2- morfolin- 4- il- etoxi)- [3,3']bipiridinil- 6- ilamina; 6'- amino- 5'- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 1- (2- pirrolidin- 1- il- etil)- 1H- [3,3']bipiridinil- 6- ona; 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 6'- (2- pirrolidin- 1- il- etoxi)- [3,3']bipiridinil- 6- ilamina; 6'- amino- 5'- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 1- [2- (1- metil- pirrolidin- 2- il)- etil]- 1H- [3,3']bipiridinil- 6- ona; (4- {6- amino- 5- [1- (2,4,6- trimetil- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2- cloro- 6- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (4- fluoro- fenil)- piridin- 2- ilamina; 6'- amino- 5'- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 1H- [3,3']bipiridinil- 6- ona; 5`- bromo- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [3,3']bipiridin- 6- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (4- dimetilamino- fenil)- piridin- 2- ilamina; 5- [1- (2,6- dicloro- 3- fluoro-

fenil)- etoxi]- 2´- metoxi- [3,3´]bipiridin- 6- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (1H- indol- 5- il)- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2,6- dicloro- fenil)- propoxi]- piridin- 3- il}- fenil)- (3,5- dimetil- piperazin- 1- il)- metanona; [4- {6- amino- 5- benciloxi- piridin- 3- il)- fenil]- (4- pirrolidin- 1- il- piperiidn- 1- il)- metanona; 3- [1- (2,6- dicloro- 3- fluoro- benciloxi)- 5- tiazol- 2- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2- fluoro- 6- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 3- (2,6- dicloro- 3- fluoro- benciloxi)- 5- (1- metil- 1H- imidazol- 2- il)- piridin- 2- ilamina; {4- [6- amino- 5- (2,4,6- trimetil- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; {4- [6- amino- 5- (2,3,5,6- tetrametil- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; {4- [6- amino- 5- (2,4,6- trifluoro- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2- fluoro- 6- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 6- amino- 5- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- N- metil- nicotidina; 6- amino- 5- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- N- (2- morfolin- 4- il- etil)- nicotidina; (4- {6- amino- 5- [1- (2,4,5- trifluoro- fenil)- propoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; (4- {6- amino- 5- [1- (6- cloro- 2- fluoro- 3- metil- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; ácido 3- (1- {2- amino- 5- [4- (4- pirrolidin- 1- il- piperidin- 1- carbonil)- fenil]- piridin- 3- iloxi}- etil)- benzoico; y sales, hidratos y solvatos farmaceuticamente aceptables de los mismos.

En otra realización- el invento proporciona un compuesto seleccionado del grupo que consta de

3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; 3- {5- amino- 6- [1- (2- cloro- 3,6- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; 3- {5- amino- 6- [1- (2- cloro- 3,6- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4- il)- benzamida; 3- {5- amino- 6- [1- (2,- cloro- 3- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; 3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 1- il- etil)- benzamida; 3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- benzamida; N- [2- (4- acetil- piperazin- 1- il)- etil- 3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- benzamida; (3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; (3-

{5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; (3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; (3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- ((S)- 2- pirrolidin- 1- il)- metanona; (3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona; (3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- ((S)- 3- amino- pirrolidin- 1- il)- metanona; ácido 4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- benzoico; 4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il))- metanona; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il))- metanona; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona; 4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4- il)- benzamida; 4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; 4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- benzamida; [2- (4- acetil- piperazin- 1- il)- etil]- 4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- benzamida; ácido 2- [4- (2- hidroxi- acetil)- piperazin- 1-]- etanosulfónico; 4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida; ácido 3- [5- amino- 6- [1- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- benzoico; {3- {5- amino- 6- [1- (3- fluoro- 2- trifluorometil- benciloxi)- pirirazin- 2- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 3- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- N- {2- [etil- (2- metoxi- etil)- amino]- etil}- benzamida; {3- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirirazin- 2- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; 3- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- N- (3- pirrolidin- 1- il- propil)- benzamida; N- [2- (4- acetil- piperazin- 1- il)- 3- [5- amino- 6-

(3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- benzamida; {4- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirirazin- 2- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; {3- {5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirirazin- 2- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; {3- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirirazin- 2- il]- fenil}- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (3- [5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; (3- [5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- (3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4- il)- benzamida; 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- benzamida; 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- morfolin- 4- il- propil)- benzamida; (3- [5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- (4- ciclopropilamino- piperidin- il)- metanona; 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- ((S)- 2- hidroxi- 3- morfolin- 4- il- propil)- benzamida; 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- ((R)- 2- hidroxi- 3- pirrolidin- 1- il- propil)- benzamida; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- piperidin- 1- il)- metanona; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- amida del ácido 2- dietilamino- etanosulfónico; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- amida del ácido 2- dimetilamino- etanosulfónico; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- amida del ácido 2- ((R- 3- hidroxi- pirrolidin- 1- il)- etanosulfónico; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- amida del ácido 2- pirrolidin- 1- iletanosulfónico; ácido (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirirazin- 2- il}- benzoico; 4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- ((R)- 2- hidroxi- 3- pirrolidin- 1- il- propil)- benzamida; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- ciclopropilamino- 1- piperidin- 1- il)- metanona; 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- ((S)- 2- hidroxi- 3- pirrolidin- 1- il- propil)- benzamida; 4- {5- amino-

6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- ((R)- 2- hidroxi- 3- morfolin- 4- il- propil)- benzamida; 4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4)- benzamida; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((S)- 2- pirrolidin- 1- metil- pirrolidin- 1- il)- metanona; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- benzamida; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- metil- 1- piperazin- 1- il)- metanona; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((3R,5S)- 3,5- dimetil- piperazin- 1- il)- metanona; ácido 4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- benzoico; (4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- benzamida; (4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; 4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4- il)- benzamida; (4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; (4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((S)- 2- pirrolidin- 1- il)- metanona; (4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; (4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (R)- 3- aminopirrolidin- 1- il)- metanona; cloruro de hidrogeno (4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((S)- 3- aminopirrolidin- 1- il)- metanona; 4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; 4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; ácido 3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- benzoico; 3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4- il)- benzamida; 3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; (3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; 3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- benzamida; (3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]-

pirazin- 2- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- pirrolidin- 1- ilpiperidin- 1- il)- metanona; N- [2- (4- acetil- piperazin- 1- il)- etil]- 4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- benzamida; N- [2- (4- acetil- piperazin- 1- il)- etil]- 3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- benzamida; (3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; 3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; (3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((S)- 3- amino- pirrolidin- 1- il)- metanona; sal de hidrocloruro (3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona; (3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; 1- (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- 3- (2- morfolin- 4- il- etil)- urea; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- amida del ácido (R)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxilico; 1- (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- 3- (2- pirrolidin- 1- il- etil)- urea; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- amida del ácido 4- metil- piperazin- 1- carboxilico; 1- (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- 3- (2- hidroxi- etil)- urea; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- amida del ácido (S)- 3- amino- pirrolidina- 1- carboxilico; 1- (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- 3- (1- metil- piperidin- 4- il)- urea; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido 4- metil- piperazin- 1- carboxilico; 1- (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}fenil)- 3- (2- hidroxi- etil)- urea; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido (S)- 3- amino- pirrolidin- 1- carboxilico; 1- (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}fenil)- 3- (1- metil- piperidin- 4- il)- urea; ácido {5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofeno- 2- carboxilico ; {5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofen- 2- il}- (4- metil- piperazin- 1- il)- metanona {5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofen- 2- il}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; {5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofen- 2- il}- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)-

metanona; {5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofen- 2- il}- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (2- morfolin- 4- il- etil)- amida del ácido 5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofeno- 2- carboxilico; trifluoroacetato 3- [(2,6- dicloro- 3- fluorofenil)- etoxi]- 5- {5- [(4- metilpiperazin- 1- il)- carbonil]piridin- 2- il}pirazin- 2- amina, 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- piridin- 4- il- pirazin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (1H- pirrol- 2)- ilamina; (6- [5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il]- tiofen- 2- il}- piridin- 3- il)- (4- metil- piperazin- 1- il)- metanona; (2- [5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- piridin- 4- il)- (4- metil- piperazin- 1- il)- metanona; (6- [5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- piridin- 2- il)- (4- metil- piperazin- 1- il)- metanona; (5- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- piridin- 3- il)- (4- metil- piperazin- 1- il)- metanona; (4- [5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- piridin- 2- il)- (4- metil- piperazin- 1- il)- metanona; 6- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- nicotinamida; 5- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- nicotinamida; 6- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- morfolin- 4- il- propil)- nicotinamida; 5- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- morfolin- 4- il- propil)- nicotinamida; (6- [5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- piridin- 3- il)- (4- isopropil- piperazin- 1- il)- metanona;

En otro aspecto, el invento proporciona un compuesto seleccionado del grupo que consta de los compuestos mostrados en la tabla 1 y sales, hidratos y solvatos farmaceuticamente aceptables del mismo.

En otro aspecto, el invento proporciona un compuesto seleccionado del grupo que consta de los compuestos mostrados en la tabla 2 y sales, hidratos y solvatos farmaceuticamente aceptables del mismo.

En otro aspecto, el invento proporciona un compuesto seleccionado del grupo que consta de los compuestos mostrados en la tabla 3 y sales, hidratos y solvatos farmaceuticamente aceptables del mismo.

En otro aspecto, el invento proporciona un compuesto seleccionado del grupo que consta de los compuestos mostrados en la tabla 4 y sales, hidratos y solvatos farmaceuticamente aceptables del mismo.

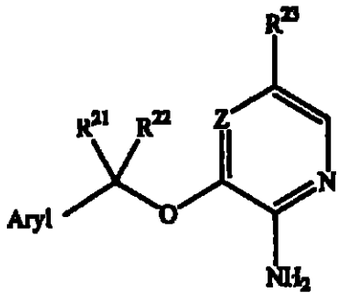
En otro aspecto, el invento proporciona un compuesto seleccionado del grupo que consta de los compuestos mostrados en la tabla 5 y sales, hidratos y solvatos farmaceuticamente aceptables del mismo.

En otro aspecto, el invento proporciona un compuesto seleccionado del grupo que consta de los compuestos mostrados en la tabla 6 y sales, hidratos y solvatos farmaceuticamente aceptables del mismo.

En otro aspecto, el invento proporciona un compuesto seleccionado del grupo que consta de los compuestos mostrados en la tabla 7 y sales, hidratos y solvatos farmaceuticamente aceptables del mismo.

En otro aspecto, el invento proporciona un compuesto seleccionado del grupo que consta de los compuestos mostrados en la tabla 8 y sales, hidratos y solvatos farmaceuticamente aceptables del mismo.

En otra realización, el invento proporciona compuestos con la siguiente estructura química (Formula 6):



(6)

en donde,

Z es CH o N;

arilo es un arilo opcionalmente fusionado o un grupo heteroarilo opcionalmente fusionado el cual es opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consta de un halógeno,- OR24, - COR24, - COOR24, - CONR24R25, - CN, - NO2, - S(O)mR24, - SO2NR24R25, perfluoroalquilo, alquilo inferior, cicloalquilo, heterociclo, alquenilo, alquinilo, arilo, - NR24R25, - NR24C(O)R25 y - NRS(O)p25;

R21 y R22 son independientemente seleccionados del grupo que consta de hidrógeno, halógeno, COR24, - COOR24, - CONR24R25, - CN, perfluoroalquilo, alquilo inferior, cicloalquilo, heterociclo, alquenilo, alquinilo, y arilo;

R23 es seleccionado del grupo que consta de:

un arilo opcionalmente fusionado, heteroarilo, grupo alicíclico o heterocíclico, opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consta de un halógeno, - (CH2)n- OR24, - COR24, - COOR24, - CONR24R25, - CN, - NO2, - S(O)mR24, - SO2NR24R25, perfluoroalquilo, - O- perfluoroalquilo, alquilo inferior, cicloalquilo, heterociclo, heeteroarilo, alquenilo, alquinilo, arilo,- (CH2)n- NR24R25, - NR24C(O)R25 y - NR24S(O)p25, en donde dichos sustituyentes de heterociclo, heteroarilo y arilo puede ser opcionalmente sustituidos por un grupo seleccionado del grupo que consta de alquilo inferior, halógeno, C(O)NR24R25, NR24R25, NR24C(O)R25 y NR24S()pR25;

- OR24, - COR24, - COOR24, - CN, - NO2, - S(O)mR24, - SO2NR24R25, perfluoroalquilo, cicloalquilo, heterociclo, alquenilo, y alquinilo;

R24 y R25 son independientemente seleccionados del grupo que consta de hidrógeno, alquilo inferior, cicloalquilo, alquenilo, alquinilo, arilo, aminoalquilo, alquilaminoalquilo, alquilaminocicloalquilo, dialquilaminoalquilo, y - (CH2)n- heterociclo, en donde dicho - (CH2)n- heterociclo puede adicionalmente se sustituido con uno o más de alquilo inferior, - (CH2)n- hidroxilo, heterociclo y - C(O)R26,

o R24 y R25 se pueden combinar para formar un anillo heterociclico de 5 a 6 miembros con uno o más heteroátomos seleccionados del grupo que consta de N, O, S(O) y SO2, dicho anillo heterocíclico de 5 a 6 miembros puede ser opcionalmente sustituido con alquilo inferior, - (CH2)n- heterociclo, cicloalquilo, halo, - (CH2)n- NR26R27, amino, - C(O)R26, - NR26- C(O)OR27 y - NR26 - C(O)R27;

en donde R26 y R27 son independientemente seleccionados del grupo que consta de hidrógeno, alquilo inferior, - (CH2)n- cicloalquilo y - C(O)- (CH2)n- OH;

excepto que cuando Z es N y R21 y R22 son H y arilo es m- clorofenilo, R23 no es piperazina;

m es 0, 1 o 2;

n es 0, 1, 2 o 3;

p es 1 o 2;

o una sal farmaceuticamente aceptable del mismo.

En un aspecto preferido de esta realización, el compuesto de la fórmula 6, R23 es arilo o heteroarilo.

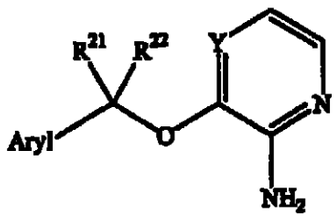
En otro aspecto preferido de esta realización, cuando Z es N, R23 no es heteroalicíclico.

En otra realización, el invento proporciona una composición farmacéutica que comprende cualquiera de los compuestos inventivos descritos en la presente. En aspectos particulares de esta realización, la composición farmacéutica comprende un compuesto de la fórmula 1, un compuesto de la fórmula 2, un compuesto de la fórmula 3, un compuesto de la fórmula 4, un compuesto de la fórmula 5, un compuesto de la fórmula 6, o una sal, hidrato o solvato farmaceuticamente aceptable del mismo, incluyendo aspectos particulares del mismo como se describió anteriormente. En otros aspectos particulares de esta realización, la composición farmacéutica comprende un compuesto seleccionado de los compuestos mostrados en la tabla 1, un compuesto seleccionado de los compuestos mostrados en la tabla 2, un compuesto seleccionado de los compuestos mostrados en la tabla 3, un compuesto seleccionado de los compuestos mostrados en la tabla 4, un compuesto seleccionado de los compuestos mostrados en la tabla 5, un compuesto seleccionado de los compuestos mostrados en la tabla 6, un compuesto seleccionado de los compuestos mostrados en la tabla 7, un compuesto seleccionado de los compuestos mostrados en la tabla 8, o una sal, hidrato o solvato farmaceuticamente aceptable del mismo.

Compuestos preferidos del invento incluyen aquellos con actividad inhibitoria de c- MET tal como se definió por uno o más de IC50, Ki, o porcentaje de inhibición. Alguien con experiencia en el estado de la técnica puede determinar con facilidad si el compuesto tiene tal actividad al realizar el ensayo apropiado. En una realización, compuestos particularmente preferidos tienen un c- MET IC50 menor que 5 uM, o menor que 2 uM, o menor que 1 uM, o menor que 500 nM, o menor que 400 nM, o menor que 300 nM, o menor que 200 nM, o menor que 100 nM, o menor que 50 nM. En otra realización, compuestos particularmente preferidos tienen un c- MET Ki menor que 5 uM o menor que 2 uM, o menor que 1 uM, o menor que 500 nM, o menor que 400 nM, o menor que 300 nM, o menor que 200 nM, o menor que 100 nM, o menor que 50 nM. En otra realización, compuestos particularmente preferidos tienen una inhibición de c- MET a 1 uM de al menos 10% o al menos 20% o al menos 30% o al menos 40% o al menos 50% o al menos 60% o al menos 70% o al menos 80% o al menos 90%.

En otra realización, el invento proporciona un proceso para preparar el compuesto de la fórmula (6), comprendiendo

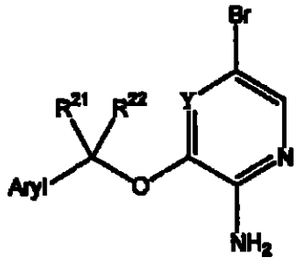
(i) bromination de un compuesto de la fórmula (a):



(a)

para proporcinar un compuesto de la fórmula (b):

y



(b)

ii. reaccionar (b) con un ácido borónico o derivado de éster de la fórmula R23B(OR)2 en presencia de un catalizador de paladio;

donde R es hidrogeno o un grupo protector de alcohol y arilo, R21, R22, y R23 son como se definieron anteriormente.

En otra realización, R23 es arilo o heteroarilo.

En otra realización el invento proporciona un método para tratar un sujeto que padece una condición para la cual se indica inhibición del receptor met con actividad tirosinaquinasa, que comprende administración al sujeto de una cantidad terapeuticamente efectiva de cualquiera de los compuestos inventivos descritos en la presente.

Las formulas químicas citadas en la presente pueden exhibir los fenomenos de tautarismo e isomerismo estructural. Este invento incluye cualquier forma tautomérica o estructural isomérica y mezclas de las mismas las cuales poseen la capacidad para modular RTK, CTK y/o actividad STK y no está limitado a cualquier forma tautomérica o estructural isomérica.

Además, las formula citadas en la presente también pueden exhibir estereoisomerismo, en el cual tales compuestos pueden adoptar una configuración R o S en los centros quirales. Así, este invento también incluye cualquier forma

estereoisómerica, sus correspondientes enantiomeros (d- y l- o isómeros (+) y (-)) y diastereoisomeros de los mismos, y mezclas de los mismos, los cuales poseen la capacidad para modular actividad RTK, CTK y/o STK y no se limita a cualquier forma estereoisomérica.

En realizaciones particulares, el compuesto es elegido a partir de los compuestos en las Tablas 1- 8.

Otra realización del invento se relaciona con un método para tratar un sujeto que padece de una condición para la cual se indica inhibición de la proteinquinasa, el cual comprende la administración al sujeto de una cantidad terapeuticamente efectiva de cualquiera de los compuestos inventivos descritos en la presente.

Otro aspecto de este invento se relaciona con un método para la modulación de la actividad catalítica de una PK al poner en contacto una PK con un compuesto de este invento o una sal farmaceuticamente aceptable del mismo.

Un aspecto adicional de este invento es que la modulación de la actividad catalítica de PKs utilizando un compuesto de este invento puede ser realizada *in vitro* o *in vivo*.

Un aspecto adicional de este invento es que la proteinquinasa cuya actividad catalítica es modulada por un compuesto de este invento es seleccionada a partir del grupo que consta de receptor con actividad proteintirosinaquinasas, tirosinaquinasas celulares y serina- treoninaquinasas.

Un aspecto de este invento es que el receptor con actividad proteintirosinaquinasa cuya actividad catalítica es modulada por un compuesto de este invento es seleccionada del grupo que consta de EGF, HER2, HER3, HER4, IR, IGF-1R, IRR, PDGFRbeta, CSFIR, C- kit, C- fms, Fik- 1R, Flk- 1R, Flk4, KDR/Flk- 1, Flt-1, FGFR- 1R, FGFR- 2R, FGFR3R, FGFR- 4R, MET, DDR- 1 y DDR- 2.

Además, un aspecto de este invento es que la tirosinquinasa celular cuya actividad catalítica es modulada mediante un compuesto de este invento es seleccionada a partir del grupo que consta de Src, Frk, Btk, Csk, Abi, ZAP70, Fes/Fps, Fak, Jak, Ack, Yes, Fyn, Lyn, Lck, Blk, Hck, Fgr y Yrk.

Otro aspecto de este invento es que la serina- treonina proteinquinasa cuya actividad catalítica es modulada mediante un compuesto de este invento es seleccionada del grupo que consta de CDK2, Raf, NEK y BUB1.

Otro aspecto de este invento se relaciona con un método para tratar o prevenir un trastorno relacionado con proteinquinasa en un organismo que comprende

administración de una cantidad terapeuticamente efectiva de cualquier compuesto inventivo descrito en la presente a un organismo, tal como un mamífeno, particularmente un humano.

Un aspecto de este invento es que el trastorno relacionado con la proteinquinasa citado anteriormente es seleccionado del grupo que consta de un trastorno relacionado con el receptor con actividad proteintirosinaquinasa, un trastorno relacionado con tirosinaquinasa celular y un trastorno relacionado con serina- treoninaquinasa.

En aún otro aspecto de este invento, el anterior trastorno relacionado con proteinquinasa es seleccionado del grupo que consta de un trastorno relacionado con Met, un trastorno relacionado con AUR2, un trastorno relacionado con ZC1, un trastorno relacionado con PDGFR, un trastorno relacionado con IGFR y un trastorno relacionado con flk.

Los trastornos relacionados proteinquinasas citados anteriormente incluyen a manera de ejemplo y sin limitación, cánceres tales como cáncer de pulmón, NSCLC (cáncer pulmonar de cédulas no pequeñas), cáncer óseo, cáncer pancreático, cáncer de piel, melanoma cutáneo o intraocular, cáncer uterino, cáncer ovárico, cáncer rectal, cáncer de la región anal, cáncer estomacal, cáncer de colon, cáncer de mama, tumores ginecológicos (ej., sarcomas uterinos, carcinoma de las trompas de Falopio, carcinoma cerviz, carcinoma de la vagina, carcinoma de la vulva), Enfermedad de Hodgkin, cáncer del esófago, cáncer del intestino delgado, cáncer del sistema endocrino (ej., cáncer de las glándulas tiroides, paratiroides o adrenal), sarcomas de tejidos blandos, cáncer de la uretra, cáncer del pene, cáncer de la próstata, leucemia crónica o aguda, tumores sólidos de la infancia, linfomas linfocíticos, cáncer de la vejiga, cáncer del riñón o uréter (ej., carcinoma de células renales, carcinoma de la pelvis renal), malignidad pediatrica, neoplasmas del sistema nervioso central (ej., linfoma del sistema nervioso central, turmores del eje espinal, glioma del tallo cerebral o adenomas pituitarios), cánceres de la sangre como leucemia mieloide aguda, leucemia mieloide crónica, etc, esófago de Barrett (síndrome pre- maligno), enfermedad neoplásica cutánea, psoriasis, micosis fungoides e hipertrofia prostática benigna, enfermedades relacionadas con diabetes tales como retinopatía diabética, isquemia retinal y neovascularización retinal, cirrosis hepática, enfermedad cardiovascular tal como ateroesclerosis, enfermedad inmunológica tal como enfermedad autoinmune y enfermedad renal. Preferiblemente, la enfermedad es cáncer tal como leucemia mieloide aguda y cáncer colorectal.

El trastorno proteinquinasa relacionado citado anteriormente también incluye trastornos seleccionados del grupo que consta de diabetes, un trastorno de híper-proliferación, trastornos hiperproliferativos del riñón, enfermedad de von Hippel-Lindau, restenosis, fibrosis, psoriasis, osteoartritis, artritis reumatoide, un trastorno inflamatorio y angiogenesis en aún otro aspecto de este invento.

Trastornos adicionales que se puede tratar o prevenir utilizando los compuestos de este invento son los trastornos inmunológicos tales como enfermedades autoinmunes (ej., SIDA, lupus, etc) y trastornos cardiovasculares tales como ateroesclerosis.

Un aspecto de este invento es que el trastorno proteinquinasa relacionado tratado o prevenido mediante la administración de un compuesto de este invento es un trastorno met quinasa relacionado.

El organismo en el cual el trastorno proteinquinasa relacionado es tratado o prevenido es un humano en aún otro aspecto de este invento.

También es un aspecto de este invento que un compuesto descrito en la presente, o su sal, puede ser combinado con otros agentes quimioterapéuticos para el tratamiento de las enfermedades y trastornos discutidos anteriormente. Por ejemplo, un compuesto o sal de este invento se puede combinar con agentes alquilantes tal como fluoracil (5- FU) solo o en ambinación adicional con leukovorin; u otros agentes alquilantes tales como, sin limitación, otros análogos de pirimidina tales como UFT, capecitabina, gemcitabina y citarabina, los sulfonatos de alquilo, ej., busulfan (utilizado en el tratamiento de leucemia granulocítica crónica),improsulfan y piposulfan; aziridinas, ej., benzodepa, carboquona, meturedepa y uredepa; etileniminas y metilmelaminas, ej., altretamina, trietilenmelamina, trietilenfosforamida, trietilentiofosforamida y trimetilolmelamina; y las mostazas de nitrógeno, ej. clorambucil (utilizada en el tratamiento de leucemia linfocítica crónica, macroglobulinemia primaria y linfoma no Hodgkin, ciclofosfamida (utilizada el tratamiento de la enfermedad de Hodgkin, mieloma múltiple, neuroblastoma, cáncer de mama, cáncer ovárico, cáncer pulmonar, tumor de Wilm y rabdomiosarcoma), estramustina, ifosfamida, novembrichina, prednimustina y mostaza de uracilo (utilizada en el tratamiento de trombocitosis primaria, linfoma no Hodgkin, enfermedad de Hodgkin y cáncer ovárico); y triazinas, ej., dacarbazina (utilizada en el tratamiento de sarcoma de tejidos blandos).

Igualmente un compuesto o sal de este invento se puede esperar tenga un efecto benéfico en combinación con otros agentes quimioterapéuticos antimetabolitos tales como, sin limitación, análogos del ácido fólico, ej., metotrexato (utilizado en el

tratamiento de leucemia linfocítica aguda, coriocarcinoma, cáncer de mama, micosis fungoide, cáncer de cabeza y cuello y sarcoma osteogénico) y pteropterina; y los análogos de purina tales como mercaptopurina y tioguanina los cuales encuentran uso en el tratamiento de leucemias granulocíticas agudas, linfocíticas agudas, y granulocíticas crónicas.

También se puede esperar que un compuesto o sal de este invento sea eficaz en combinación con agentes quimioterapéuticos basados en productos naturales tales como, sin limitación, los alcaloides vinca, ej. vinblastina (utilizado en el tratamiento de cáncer de mama y cáncer testicular), vincristina y vindesina; las epipodofilotoxinas, ej., etoposide y teniposide, ambas útiles en el tratamiento de cáncer testicular y sarcoma de Kaposi; los agentes quimioterapéuticos antibióticos, ej., daunorubicina, doxorubicina, epirubicina, mitomicina (utilizados para tratar cáncer pancreático, de estómago, cérvix, colon, mama, y vejiga), dactinomicina, temozolomida, plicamicina, bleomicina (utilizados en el tratamiento de cáncer de piel, esófago y tracto genitourinario); y los agentes quimioterapéuticos enzimáticos tales como L- asparaginasa.

Además, se espera que un compuesto o sal de este invento tenga un efecto benéfico utilizado en combinación con complejos de coordinación de platino (cisplatina, etc.); ureas sustituidas tal como hidroxiurea; derivados de metilhidrazina, ej., procarbazina; supresores adrenocorticales, ej., mitotano, aminoglutetimida; y hormona y antagonistas de hormonas tales como los adrenocorticosteroides (ej., prednisona), progestinas (ej., hidroxiprogesterona, caproato); estrógenos (ej., dietilstilbesterol); antiestrogenos tales como tamoxifen; andrógenos, ej., propionato de testosterona; e inhibidores de aromatasa tales como anastrozol.

Finalmente, la combinación de un compuesto de este invento se espera sea particularmente efectiva en combinación con mitoxantrona o paclitaxel para el tratamiento de cánceres de tumores sólidos o leucemias tales como, sin limitación, leucemia mielógena aguda (no linfocítica).

El anterior método se puede realizar en combinación con un agente quimioterapéutico seleccionado del grupo que consta de inhibidores mitóticos, agentes alquilantes, antimetabolitos, inhibidores de ciclo celular, enzimas, inhibidores de topoisomersa, modificadores de respuesta biológica, anti- hormonas, agentes antiangiogénicos tales como MMP- 2, MMP- 9 e inhibidores de la COX- 2, y anti-andrógenos. .

Ejemplos de inhibidores útiles de la COX- II incluyen CELEBREX™ (alecoxib), valdecoxib, y rofecoxib. Ejemplos de inhibidores útiles de matriz metaloproteinasa son descritos en WO 96/33172 (publicada en Octubre 24 de 1996), WO 96/27583 (publicada en Marzo 7 de 1996), Solicitud de Patente Europea No. 97304971.1 (registrada en Julio 8 de 1997), Solicitud de Patente Europea No. 99308617.2 (registrada en Octubre 29 de 1999), WO 98/07697 (publicada en Febrero 26 de 1998), WO 98/03516 (publicada en Enero 29 de 1998), WO 98/34918 (publicada en Agosto 13 de 1998), WO 98/34915 (publicada en Agosto 13 de 1998), WO 98/33768 (publicada en Agosto 6 de 1998), WO 98/30566 (publicada en Julio 16 de 1998), Publicación de Patente Europea 606, 046 (publicada en Julio 13 de 1994), Publicación de Patente Europea 931, 788 (publicada en Julio 28 de 1999), WO 90/05719 (publicada en Mayo 31 de 1990), WO 99/52910 (publicada en Octubre 21 de 1999), WO 99/52889 (publicada en octubre 21 de 1999), WO 99/29667 (publicada en Junio 17 de 1999), Solicitud Internacional PCT No. PCT/B98/01113 (registrada en Julio 21 de 1998), Solicitud de Patente Europea No. 993022321 (registrada en Marzo 25 de 1999), Solicitud de Patente de Gran Bretaña No. 9912961.1 (registrada en Junio 3 de 1999), Solicitud Provisional Americana No. 60/148,464 (registrada en Agosto 12 de 1999), Patente Americana 5, 863,949 (publicada en Enero 26 de 1999), Patenten Americana 5, 861,510 (publicada en Enero 19 de 1999); y Publicación de Patente Europea 780,386 (publicada en Junio 25 de 1997), todas incorporadas en la presente como referencia en su totalidad. Los inhibidores preferidos de MMP- 2 y MMP- 9 son aquellos que tienen poca o nada de actividad la cual inhibe MMP- 1. Más preferidos son aquellos que selectivamente inhiben MMP- 2 y/o MMP- 9 con relación a otras matriz-metaloproteinasas (es decir, MMP- 1, MMP- 3, MMP- 4, MMP- 5, MMP- 6, MMP- 7, MMP- 8, MMP- 10, MMP- 11, MMP- 12, y MMP- 13).

Algunos ejemplos específicos de inhibidores MMP útiles en el presente invento son AG- 3340, RO 32- 3555, RS 13- 0830, y los compuestos expuestos en la siguiente lista:

Acido 3- [[4- (4- fluoro- fenoxi)- bencenosulfonil]- (1- hidroxicarbomil- ciclopentil)- amino]- propionico;

Hidroxiamida del ácido 3- exo- 3- [4- (4- fluoro- fenoxi)- bencenosulfonilamino]- 8- oxa- biciclo[3.2.1]octano- 3- carboxílico;

Hidroxiamida del ácido (2R, 3R) 1- [4- (2- cloro- 4- fluoro- benciloxi)- bencenosulfonil]- 3- hidroxi- 3- metil- piperidina- 2- carboxílico.

Hidroxiamida del ácido de 4- [4- (4- fluoro- fenoxi)- bencenosulfonilamino]- tetrahidro- piran- 4- carboxílico

Acido 3- [[4- (4- fluoro- fenoxi)- bencenosulfonil]- (hidroxicarbamoil- ciclobutil)- amino]- propiónico;

Hidroxiamida del ácido 4- [4- (4- cloro- fenoxi)- bencenosulfonilamino]- tetrahidro- piran- 4- carboxílico

Hidroxiamida del ácido 3- [4- (4- cloro- fenoxi)- bencenosulfonilamino]- tetrahidro- piran- 3- carboxílico

Hidroxiamida del ácido (2R, 3R) 1- [4- (4- fluoro- 2- metil- benciloxi)- bencenosulfonil]- 3- hidroxi- 3- metil- piperidina- 2- carboxílico.

Acido 3- [[4- (4- fluoro- fenoxi)- bencenosulfonil]- (1- hidroxicarbamoil- 1- metil- etil)- amino]- propiónico;

Acido 3- [[4- (4- fluoro- fenoxi)- bencenosulfonil]- (4- hidroxicarbamoil- tetrahidro- piran- 4- il)- amino]- propiónico;

Hidroxiamida del ácido 3- exo- 3- [4- (4- cloro- fenoxi)- bencenosulfonilamino]- 8- oxa- biciclo[3.2.1]octano- 3- carboxílico

Hidroxiamida del ácido 3- endo- 3- [4- (4- fluoro- fenoxi)- bencenosulfonilamino]- 8- oxa- biciclo[3.2.1]octano- 3- carboxílico; y

Hidroxiamida del ácido 3- [4- (4- fluoro- fenoxi)- bencenosulfonilamino]- tetrahidro- furan- 3- carboxílico

y sales farmaceuticamente aceptables, solvatos y profármacos de dichos compuestos.

Otros agentes anti- angiogencsis, incluyendo inhibidores de la COX- II y otros inhibidores MMP, también se pueden utilizar en el presente invento.

Un compuesto del invento también se puede utilizar en combinación con inhibidores de transducción de señales, tales como agentes que pueden inhibir respuestas EGFR (receptor del factor de crecimiento epidérmico), tales como anticuerpos EGFR, anticuerpos EGF, y moleculas que son inhibidores EGFR; inhibidores VEGF (factor de crecimiento endotelial vascular); e inhibidores de receptores erbB2, tales como moléculas orgánicas o anticuerpos que se fijan al receptor erbB2, por ejemplo, HERCEPTIN (Genentech, Inc. San Francisco Sur, California, USA). Los inhibidores EGFR son descritos en, por ejemplo WO 95/19970 (publicada en julio 27 de 1995), WO 98/14451 (publicada en Abril 9 de 1998), WO 98/02434 (publicada en Enero 22 de 1998), y la Patente Americana 5.747.498 (publicada en Mayo 5 de 1998), y tales sustancias se pueden utilizar en el presente invento como se describe en la presente.

Los agentes inhibidores de EGFR incluyen, pero no están limitados a, los anticuerpos monoclonales C225 y anti- EGFR 22Mab (ImClone Systmes Incorporated de New Tork, New York, USA), los compuestos ZD- 1839 (AstraZeneca), BIBX- 1382 (Boehringer Ingelheim), MDX- 447 (Medarex Inc. de Annandale, New Jersey, USA), y OLX- 103 (Merck & Co. de Whitehouse Station, New Jersey, USA), VRCTC- 310 (Ventech Research) y toxina de efusión EGF (Seragen Inc. Hopkinton, Massachusettes).

Estos y otros agentes inhibidores de EGFR se pueden utilizar en el presente invento.

Los inhibidores VEGF, por ejemplo 3- (2,4- dimetilpirrol- 5- il)metileno- 2- indolinona, (2- dietilamino- etil)- amida del ácido 5- (5- fluoro- 2- oxo- 1,2- dihidro- indol- 3- ilidenmetil)- 2,4- dimetil- 1H- pirrola- 3- carboxílico, ácido 3- [2,4- dimetil- 5- oxo- 1,2- dihidroindol- 3- ilidenmetil)- 1H- pirrol- 3- il- propiónico (Sugen Inc. de South San Francisco, Calid, USA), también se pueden combinar con un compuesto inventivo descrito en la presente. Los inhibidores VEGF son descritos por ejemplo en WO 99/24440 (publicada en Mayo 20 de 1999), Solicitud Internacional PCT PCT/IB99/00797 (registrada en Mayo 3 de 1999), en WO 95/21613 (publicada en Agosto 17 de 1995), WO 99/61422 (publicada en Diciembre 2 de 1999), Patente Americana 5.834.504 (publicada en Noviembre 10 de 1998), WO 98/50356 (publicada

en Noviembre 12 de 1998), Patente Americana 5.883.113 8publicada en Marzo 16 de 1999), Patente Americana 5.886.029 (publicada en Marzo 23 de 1999), Patente Americana 5.792.783 (publicada en Agosto 11 de 1998), WO 99/10349 (publicada en Marzo 4 de 1999), WO 97/32856 (publicada en septiembre 12, de 1997), WO 97/22596 (publicada en Junio 26 de 1997), WO 98/54093 (publicada en diciembre 3 de 1998), WO 98/02438 (publicada en Enero 22 de 1998), WO 99/16755 (publicada en Abril 8 de 1999), y WO 98/02437 (publicada en Enero 22 de 1998), todas incorporadas en la presente como referencia en su totalidad. Otros ejemplos de algunos inhibidores VEGF específicos son IM862 (Cytran. Inc. de Kirkland, Washington, USA); anticuerpo monoclonal anti- VEGF de Genentech, Inc. de San Fracisco del Sur, California; y angiozima, una ribosima sintética de Ribozyme (Boulder, Colorado) y Chiron (Emeryville, California). Estos y otros inhibidores VEGF pueden ser utilizados en el presente invento como se describe en la presente.

Los inhibidores de receptores ErbB2, tales como GW- 282974 (Glaxo Wellcome pic), y los anticuerpos monoclonales AR- 209 (Aronex Pharmaceuticals Inc. de Woodlands, Texas, USA) y 2B- 1 (Chiron), pueden ser combinados con un compuesto de cualquiera de los compuestos inventivos descritos en la presente, por ejemplo aquellos descritos en WO 98/02434 (publicada en Enero 22 de 1998), WO 99/35146 (publicada en Julio 15 de 1999), WO 99/35132 (publicada en Julio 15 de 1999), WO 98/02437 (publicada en Enero 22 de 1998), WO 97/13760 (publicada en Abril 17 de 1997), WO 95/19970 (publicada en Julio 27 de 1995), Patente Americana 5.587.458 (publicada en Diciembre 24 de 1996), y Patente Americana 5.877.305 (publicada en Marzo 2 de 1999), cada una de estas incorporada en la presente como referencia en su totalidad. Los inhibidores de receptores de ErnB2 útiles en el presente invento también son descritos en la Solicitud Provisional Americana No. 60/117.341, registrada en Enero 27 de 1999, y en la Solicitud Provisional Americana No. 60/117.346 registrada en Enero 27 de 1999, ambas incorporadas en la presente como referencia en su totalidad. Los compuestos inhibidores de receptores erbB2 y la sustancia descrita en las solicitudes PCT antes mencionadas, patentes americanas, y solicitudes americanas provisionales, así como también otros compuestos y sustancias que inhiben el receptor erbB2, se pueden utilizar con los compuestos inventivos descritos en la presente.

Los compuestos inventivos descritos en la presente también se pueden utilizar con otros agentes útiles en el tratamiento de crecimiento celular anormal o cáncer, los cuales incluyen, pero no están limitados a, agentes capaces de aumentar respuestas

inmunes antitumorales, tales como anticuerpos CTLA4 (antigeno asociado al linfocito citotóxico 4), y otros agentes capaces de bloquear CTLA4; y agentes anti- proliferativos tales como otros inhibidores de la farnesil proteintransferasa, por ejemplo los inhibidores de la farnesil proteintransferasa descritos en las referencias citadas en la sección "Fundamento", *supra.* Anticuerpos CTLA4 específicos que pueden ser utilizados en el presente invento incluyen aquellos descritos en la Solicitud Provisional Americana 60/113.647 (registrada en Diciembre 23 de 1998) la cual es incorporada en la presente como referencia en su totalidad, sin embargo otros anticuerpos CTLA4 se pueden utilizar en el presente invento.

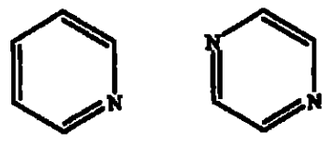
El anterior método también se puede realizar en combinación con terapia de radiación, en donde la cantidad del compuesto inventivo en combinación con la terapia de radiación es efectiva para tratar las anteriores enfermedades. Las técnicas para administrar terapia de radiación son conocidas en el estado de la técnica, y estas técnicas se pueden utilizar en la terapia de combinación descrita en la presente. La administración del compuesto del invento en esta terapia de combinación se puede determinar como se describe en la presente.

Otro aspecto del invento está dirigido al uso de cualquiera de los compuestos descritos en la presente in la prepración de un medicamento, el cual es útil en el tratamiento de una enfermedad mediada por actividad met quinasa anormal, tal como cáncer.

DESCRIPCION DETALLADA

Definiciones

Los términos piridina y pirazina se refieren a las siguientes estructuras respectivamente:



"Sal farmaceuticamente aceptable" o "sal farmaceuticamente aceptable de la misma" se refieren a aquellas sales que retienen la efectividad biológica y propiedades de las bases libres y las cuales son obtenidas mediante reacción con ácidos orgánicos o inorgánicos, tales como ácido clorhídrico, ácido hidrobrómico, ácido hidroyodico, ácido sulfúrico, ácido nítrico, ácido fosfórico, ácido metanosulfónico, sido etanosulfónico,

ácido p- toluenosulfónico, ácido salicílico, ácido acético, ácido bencenosulfónico, (besilato) ácido benzoico, ácido canforsulfónico, ácido cítrico, ácido fumárico, ácido glucónico, ácido glutámico, ácido isetiónico, ácido láctico, ácido maléico, ácido málico, ácido mandélico, ácido múcico, ácido pamóico, ácido pantoténico, ácido succínico, ácido tartárico, y similares.

Una "composición farmaceutica" se refiere a una mezcla de uno más compuestos descritos en la presente, o sales fisiológicamente aceptables de los mismos, con otros componentes químicos, tales como vehículos y excipientes fisiológicamente aceptables. El propósito de una composición farmaceutica es facilitar la administración de un compuesto a un organismo.

Como se utiliza en la presente, un "vehículo fisiológicamente aceptable" se refiere a un vehículo o diluyente que no produce irritación significativa a un organismo y no anula la actividad biológica y propiedades del compuesto administrado.

Un "excipiente" se refiere a una sustancia inerte agregada a una composición farmaceutica para facilitar adicionalmente la administración del compuesto. Ejemplos sin limitación, de excipientes incluyen carbonato de calcio, fosfato de calcio, varios azucares y tipos de almidón, derivados de celulosa (incluyendo celulosa microcristalina), gelatina, aceites vegetales, glicoles de polietileno, diluyentes, agentes de granulación, lubricantes, aglomerantes, agentes desintegrantes, y similares.

Los compuestos que tienen la misma fórmula molecular pero difieren en la naturaleza o secuencia de unión de sus átomos o la disposición de sus átomos en espacio se denominan "isómeros". Los isómeros que difieren en la disposición de sus átomos en espacio se denominan "estereoisómeros". Los estereoisómeros que no son imágenes idénticas entre sí se denominan "diastereomeros" y aquellos que no son imágenes idénticas superimponibles entre si se denominan "enantiómeros". Cuando un compuesto tiene un centro asimétrico, por ejemplo, este está unido a cuatro grupos diferentes, un par de enantiómeros es posible. Un enantiomero se puede caracterizar por la configuración absoluta de su centro asimétrico y es descrita por las reglas de secuenciamiento R- y S- de Cahn y Prelog, o por la manera en la cual la molécula gira el plano de luz polarizada y designada como dextrorotatorio o levorotario (es decir, como isómeros (+) o (-), respectivamente). Un compuesto quiral puede existir ya sea como un enantiomero individual o como una mezcla del mismo. Una mezcla que contiene proporciones iguales de los enantiómeros se llama una "mezcla racémica".

Los compuestos de este invento pueden poseer uno o más centros asimétricos; por lo tanto tales compuestos pueden ser producidos como estereoisómeros (R)- o (S)- individuales o como mezclas de los mismos. A menos que se indique lo contrario, la descripción o denominación de un compuesto particular en la especificación y reivindicaciones pretende incluir tanto los enantiómeros individuales como las mezclas, racémicas u otras, de los mismos. Los métodos para la determinación de estereoquimica y la separación de estereoisomeros son bien conocidos en el estado de la técnica (*ver* discusión en Capitulo 4 de "Química Orgánica Avanzada", cuarta edición J. March. John Wiley e Hijos, Nueva York, 1992).

Los compuestos del presente invento pueden exhibir fenómenos de tautomerismo e isomerismo estructural. Este invento incluye cualquier forma isomérica tautomérica o estructural y mezclas de la misma que poseen la capacidad para modular la actividad RTK, CTK y/o STK y no se limita a cualquier forma tautomérica o estructural.

Se contempla que un compuesto inventivo tal como se describe en la presente sería metabolizado por enzimas en el cuerpo del organismo tal como un ser humano para generar un metabolito que pueda modular la actividad de las proteínas quinasas. Tales metabolitos están dentro del alcance del presente invento.

Como se utiliza en la presente "PK" se refiere al receptor con actividad proteintirosinaquinasa (RTKs), tirosinaquinasa "celular" y serina- treoninaquinasas (STKs).

El término "método" se refiere a las formas, medios, técnicas y procedimientos para realizar una tarea dada incluyendo, pero sin limitación a, aquellas formas, medios, técnicas y procedimientos ya sea conocidos o fácilmente desarrollados a partir de formas medios, técnicas y procedimientos conocidos por practicantes de las artes químicas, farmacéuticas, biológicas, bioquímicas y médicas.

Como se utiliza en la presente, el término "modulación" se refiere a la alteración de la actividad catalítica de las RTKs, CTKs y STKs. En particular, modulación se refiere a la alteración de la actividad catalítica de las RTKs, CTKs y STKs, preferiblemente la activación o inhibición de la actividad catalítica de las RTKs, CTKs y STKs, dependiendo de la concentración del compuesto o sal al cual la RTK, CTK o STK es expuesta o, más preferiblemente, la inhibición de la actividad catalítica de las RTKs, CTKs y STKs.

El término "actividad catalítica" se refiere a la tasa de fosforilación de tirosina

bajo la influencia, directa o indirecta de RTKs y/o CTKs o la fosforilación de serina y treonina bajo la influencia, directa o indirecta, de STKs.

El término "entrar en contacto" se refiere a la unión de un compuesto de este invento y una PK objetivo en una forma tal que el compuesto puede afectar la actividad catalítica de la PK, ya sea directamente, es decir interactuando con la quinasa misma, o indirectamente, es decir interactuando con otra molécula sobre la cual la actividad catalítica de la quinasa es dependiente. Tal "contacto" puede ser realizado "in vitro", es decir, en un tubo de ensayo, un plato Petri o similares. En un tubo de ensayo, el contacto puede involucrar solamente un compuesto y una PK de interés o puede involucrar todas las células. Las células también pueden ser mantenidas o cultivadas en platos de cultivo celular y entrar en contacto con un compuesto en ese ambiente. En este contexto, la capacidad de un compuesto particular para afectar un trastorno relacionado con PK, es decir, el IC50 del compuesto, definido más adelante, puede ser determinada antes del uso de los compuestos in vivo con organismos vivientes más complejos. Para las células fuera del organismo, existen múltiples métodos, y son bien conocidos por aquellos con habilidad en el estado de la técnica, para obtener las PKs en contacto con los compuestos incluyendo, pero sin limitar a microinyección celular directa y numerosas técnicas vehiculares transmembranales.

"In vitro" se refiere a procedimientos realizados en un ambiente artificial tal como, ej., sin limitación, en un tubo de ensayo o medio de cultivo. Alguien con habilidad entenderá que, por ejemplo, una PK aislada se puede poner en contacto con un modulador en una ambiente in vitro. Alternativamente, una célula aislada puede entrar en contacto con un modulador en un ambiente in vitro.

"In vivo" se refiere a procedimientos realizados dentro de un organismo vivo tal como, sin limitación, un ratón, rata, conejo, ungulado, bovino, equino, porcino, canino, fenilo, primate, o humano.

Como se utiliza en la presente "trastorno relacionado con PK," "trastorno promovido por PK," y "actividad PK anormal" todos se refieren una condición caracterizada por actividad catalítica inapropiada, donde la PK particular puede ser una RTK, una CTK o una STK. La actividad catalítica inapropiada puede surgir como resultado de: expresión PK en celulas que normalmente no expresan PKs, (2) expresión PK aumentada que lleva a proliferación, diferenciación y/o crecimiento celular indeados, o, (3) expresión PK disminuida que lleva a reducciones indeseadas en proliferación, diferenciación y/o crecimiento celular. Sobre- actividad de una PK se

refiere a la amplificación del gen que codifica una PK particular o producción de un nivel de actividad PK el cual puede estar relacionado con un trastorno de proliferación, diferenciación y/o crecimiento celular (es decir, a medida que el nivel de PK aumenta, la severidad de uno o más de los síntomas del trastorno celular aumento). Infra-actividad es, naturalmente, lo inverso, en donde la severidad de uno o más síntomas de un trastorno celular aumenta a medida que el nivel de la actividad PK disminuye.

Como se utiliza en la presente, los términos "prevenir", "previniendo" y "prevención" se refieren a un método para impedir que un organismo adquiera un trastorno PK relacionado en primer lugar.

Como se utiliza en la presente "tratar", "tratando" y "tratamiento" se refieren a un método para aliviar o anular un trastorno celular mediado por PK y/o sus síntomas concurrentes. Con respecto particularmente al cáncer, estos términos simplemente significan que la expectativa de vida de un individuo afectado con un cáncer será aumentada o que uno o más de los síntomas de la enfermedad serán reducidos.

El término "organismo" se refiere a cualquier entidad viviente compuesta de al menos una célula. Un organismo viviente puede ser tan simple como, por ejemplo, una célula eucariótica, tan complejo como un mamífero. En un aspecto preferido, el organismo es un mamífero. En un aspecto particularmente preferido, el mamífero es un ser humano.

El término "cantidad terapéuticamente efectiva" como se utiliza en la presente se refiere a la cantidad del compuesto administrado la cual aliviará un en alguna medida uno o más de los síntomas del trastorno tratado. En referencia al tratamiento del cáncer, una cantidad terapéuticamente efectiva se refiere a aquella cantidad la cual tiene el efecto de:

(1) reducir el tamaño del tumor;

(2) inhibir (es decir, retardar en alguna medida, preferiblemente detener) la metástasis tumoral;

(3) inhibir en alguna medida (es decir, retardar en alguna medida, preferiblemente detener) crecimiento tumoral, y/o,

(4) aliviar en alguna medida (o, preferiblemente, eliminar) uno o más síntomas asociados con el cáncer.

"Monitorear" significa observar o detectar el efecto de colocar en contacto un compuesto en con una célula que expresa una PK particular. El efecto observado o detectado puede ser un cambio en fenotipo celular, y en la actividad catalítica de una PK

o un cambio en la interacción de una PK con una pareja de unión natural. Las técnicas para observar o detectar tales efectos son bien conocidas en el estado de la técnica. Por ejemplo, la actividad catalítica de una PK se puede observar al determinar la tasa o cantidad de fosforilación de una célula objetivo.

La referencia a los compuestos del invento incluye sales, solvatos e hidratos farmaceuticamente aceptables de los mismos.

"Fenotipo celular" se refiere a la apariencia exterior de una célula o tejido o la función biológica de la célula o tejido. Ejemplos, sin limitación, de un fenotipo celular son tamaño celular, crecimiento celular, proliferación celular, diferenciación celular, supervivencia celular, apoptosis, y absorción de nutrientes y uso. Tales características fenotípicas son medibles mediante técnicas bien conocidas en el estado de la técnica.

"Pareja de unión natural" se refiere a un polipeptido que se une a una PK particular en una célula. Las parejas de unión natural pueden jugar un papel en la propagación de una señal en un proceso de transducción de señales mediadas por PK. Un cambio en la interacción de la pareja de unión natural con la PK puede manifestarse como una concentración aumentada o reducida del complejo PK/las parejas de unión natural y, como resultado, en un cambio observable en la capacidad de la PK para mediar la transducción de señales.

Como se utiliza en la presente, "administrar" o "administración" se refiere a la liberación de un compuesto o sal del presente invento o de una composición farmacéutica que contiene un compuesto o sal de este invento a un organismo para el propósito de prevención o tratamiento de un trastorno relacionado con PK.

Una "composición farmacéutica" se refiere a una mezcla de uno o más compuestos descritos en la presente, o sales o profármacos farmaceuticamente aceptables de los mismos, con otros componentes químicos, tales como excipientes farmaceuticamente aceptables. El propósito de una composición farmacéutica es facilitar la administración de un compuesto a un organismo.

Un "excipiente farmacéuticamente aceptable" se refiere a una sustancia inerte agregada a una composición farmacéutica para facilitar adicionalmente la administración de un compuesto. Ejemplos, sin limitación, de excipientes incluyen carbonato de calcio, fosfato de calcio, varios azúcares y tipos de almidón, derivados de celulosa, gelatina, aceites vegetales y glicoles de polietileno.

Como se utiliza en la presente, el término "sal farmacéuticamente aceptable" se refiere a aquellas sales las cuales retienen la efectividad biológica y propiedades del

compuesto precursor. Tales sales incluyen:

(i) sal de adición ácido la cual es obtenida mediante reacción de la base libre del compuesto precursor con ácidos inorgánicos tales como ácido clorhídrico, ácido hidrobrómico, ácido nítrico, ácido fosfónico, ácido sulfúrico, y ácido perclórico y similares, o con ácidos orgánicos tales como ácido acético, acido oxálico, (D) o (L) ácido maléico, acido malico, acido metanosulfónico, acido etanosulfónico, ácido p-toluenosulfónico, ácido salicílico, ácido tartárico, ácido cítrico, acido succinico o acido malónico y similares, preferiblemente ácido clorhídrico o (L)- málico; o

(2) sales formadas cuando un protón acídico presente en el compuesto precursor es reemplazado por un ion metálico, ejemplo, un ion de metal alcalino, un ion alcalinoterreo, o un ión de aluminio; o coordenadas con una base orgánica tal como etanolamina, dietanolamina, trietanolamina, trometamina, N- metilglucamina, y similares.

Los compuestos inventivos descritos en la presente también pueden actuar como un profármaco. Un "profármaco" se refiere a un agente el cual es convertido en el fármaco precursor in vivo. Los profármacos a menudo son útiles puesto que en algunas situaciones, pueden ser más fáciles de administrar que el fármaco precursor. Estos pueden, por ejemplo, ser biodisponibles mediante administración oral mientras que el fármaco precursor no. El profármaco también puede tener solubilidad mejorada en composiciones farmacéuticas sobre el fármaco precursor.

Las PKs cuya actividad catalítica está modulada por los compuestos de este invento incluyen tirosinaquinasas de las cuales hay dos tipos, tirosinaquinasas receptoras (RTKs) y tirosinaquinasas celulares (CTKs), y serina- treoninaquinasas (STKs). La transducción de señales mediada por RTK es iniciada por la interacción extracelular con un factor de crecimiento específico (ligando), seguida por la dimerización de receptores, estimulación transitoria de la actividad intrínseca de la tirosina proteinquinasa y fosforilación. Los sitios de unión son creados así para moléculas de transducción de señales intracelulares y llevan a la formación de complejos con un espectro de moléculas de señalización citoplásmica que facilitan la respuesta celular apropiada (ej., división celular, efectos metabólicos sobre el microambiente extracelular, etc.). Ver, Schlessinger y Ullrich, 1992, Neuron 9:303-391.

Se ha mostrado que los sitios de fosforilación de tirosina sobre receptores de factor de crecimiento funcionan como sitios de unión de alta afinidad para dominios

SH2 (homologia src) de moléculas de señalización. Fantl, 1992, Cell 69:413- 423, Songyang, 1994, Cell, Mol. Cell. Biol. 14:2777- 2785), Songyang, 1993, Cell 72:767- 778, y Koch, 1991, science 252:668- 678. Se han identificado varias proteínas de sustrato intracelular que se asocian con RTKs. Éstas se pueden dividir en dos grupos principales: (1) substratos que tienen un dominio catalítico, y (2) substratos que carecen de tal dominio pero que sirven como adaptadores y se asocian con moléculas catalíticamente activas. Songyang, 1993, Cell 72:767- 778. La especificidad de las interacciones entre receptores y dominios SH2 de sus substratos es determinada mediante los residuos aminoácidos que circundan de manera inmediata el residuo de tirosina fosforilada. Las diferencias en las afinidades de unión entre dominios SH2 y las secuencias aminoácidas que circundan los residuos de fosfotirosina sobre receptores particulares son consistentes con las diferencias observadas en sus perfiles de fosforilación de substratos. Songyang 1993, Cell 72:767- 778. Estas observaciones indican que la función de cada RTK es determinada no solamente por su patrón de expresión y disponibilidad de ligandos sino también por la disposición de las rutas de transducción de señales corriente abajo que son activadas por un receptor particular. Así, la fosforilación proporciona un paso regulador importante que determina la selectividad de rutas de señalización reclutadas por receptores específicos de factor de crecimiento, así como también receptores de factor de diferenciación.

Las STKs, principalmente citosólicas, afectan la bioquímica interna de la célula, a menudo como una respuesta línea abajo a un evento PTK. Las STKs han sido implicadas en el proceso de señalización el cual inicia la síntesis de ADN y mitosis subsecuente que lleva a proliferación celular.

Así, la transducción de señales PK resulta en, entre otras respuestas, proliferación, diferenciación, crecimiento y metabolismo celular. La proliferación celular anormal puede resultar en una amplia gama de trastornos y enfermedades, incluyendo el desarrollo de neoplasia tales como carcinoma, sarcoma, glioblastoma y hemangioma, trastornos tales como leucemia, psoriasis, aterosclerosis, artritis y retinopatía diabética y otros trastornos relacionados con angiogenesis no controlada y/o vasculogenesis.

No se requiere un entendimiento preciso del mecanismo mediante el cual los compuestos de este invento, en particular, los compuestos generados in vivo a partir de los compuestos del invento, inhiben las PKs con el objeto de practicar el presente invento. Sin embargo, mientras no se está limitado en la presente a algún mecanismo

particular o teoría, se cree que los compuestos interactúan con los aminoácidos en la región catalítica de las PKs. Las PKs típicamente poseen una estructura bi- lobulada en donde ATP parece unirse en la región hendida entre los dos lóbulos en una región donde los aminoácidos son conservados entre las PKs. Se cree que los inhibidores de las PKs se unen mediante interacciones no covalentes tal como enlaces de hidrógeno, fuerzas van der Waals, interacciones iónicas en la misma región general donde el ATP antes mencionado se une a las PKs. Más específicamente, se cree que los compuestos de este invento se unen en el espacio general normalmente ocupado por el anillo de adenina de ATP.

En otro aspecto, la proteinquinasa, la actividad catalítica de la cual es modulada por contacto con un compuesto de este invento, es una proteintirosinaquinasa , más particularmente, un receptor con actividad proteintirosinaquinasa. Entre los receptores con actividad proteintirosinaquinasa cuya actividad catalítica puede ser modulada con un compuesto de este invento, o sal del mismo, están sin limitación, aquellos seleccionados del grupo que consta de Met, Flk, FGFR, PDGFR, HER, IR, IGF, IRR, CSFIR, C- Kit, C- fms, fit. En un aspecto preferido, el receptor con actividad proteintirosinaquinasa cuya actividad catalítica puede ser modulada con un compuesto de este invento, o sal del mismo.

La proteintirosinaquinasa cuya actividad catalítica es modulada por contacto con un compuesto de este invento, o sal del mismo, también puede ser un receptor sin actividad proteintirosinaquinasa o celular (CTK). Así, la actividad catalítica de CTKs tales como, sin limitación, Src, Frk, Btk, Csk, Abl, ZAP70, Fes, Fps, Fak, Jak, Ack, Yes, Fyn, Lyn, Lck, Blk, Hck, Fgr, Aur2 y Yrk puede ser modulada por contacto con un compuesto o sal de este invento.

Aún otro grupo de OKs las cuales pueden tener su actividad catalítica modulada por contacto con un compuesto de este invento son protein- serina- treoninaquinasas tales como, sin limitación, CDK2, Raf, NEK (incluyendo NEK 4a, NEK 4b, NEK 5 y NEK 6) y BUB1.

En otro aspecto, este invento se relaciona con un método para tratar o prevenir un trastorno PK relacionado mediante administración de una cantidad terapeuticamente efectiva de un compuesto de este invento, o sal del mismo, a un organismo.

También un aspecto de este invento es que la composición farmaceutica que contiene el compuesto de este invento, o sal del mismo, es administrada a un organismo para el propósito de prevenir o tratar un trastorno PK- relacionado.

Por lo tanto el invento está dirigido a compuestos que modulan la transducción de señales PK al afectar la actividad enzimática de RTKs, CTKs y/o STKs, interfiriendo así con las señales transducidas por tales proteinas. Más particularmente, el presente invento está dirigido a compuestos que modulan rutas de transducción de señales mediadas por RTK, CTK y/o STK como un enfoque terapeutico para curar muchas clases de tumores sólidos, incluyendo pero sin limitar a carcinomas, sarcomas incluyendo sarcoma de Kaposi, eritroblastoma, meningioma, astrocitoma, melanona y mioblastoma, cánceres tales como cáncer de pulmón, NSCLC (cáncer pulmonar de cédulas no pequeñas), cáncer óseo, cáncer pancreático, cáncer de piel, cáncer de cabeza de y cuello, melanoma cutáneo o intraocular, cáncer uterino, cáncer ovárico, cáncer rectal, cáncer de la región anal, cáncer estomacal, cáncer de colon, cáncer de mama, tumores ginecológicos (ej., sarcomas uterinos, carcinoma de las trompas de Falopio, carcinoma del endometrio, carcinoma cerviz, carcinoma de la vagina, carcinoma de la vulva), Enfermedad de Hodgkin, cáncer del esófago, cáncer del intestino delgado, cáncer del sistema endocrino (ej., cáncer de las glándulas tiroides, paratiroides o adrenal), sarcomas de tejidos blandos, cáncer de la uretra, cáncer del pene, cáncer de la próstata, leucemia crónica o aguda, tumores sólidos de la infancia, linfomas linfocíticos, cáncer de la vejiga, cáncer del riñón o uréter (ej., carcinoma de células renales, carcinoma de la pelvis renal), malignidad pediatrica, neoplasmas del sistema nervioso central (ej., linfoma del sistema nervioso central, turmores del eje espinal, glioma del tallo cerebral o adenomas pituitarios), cánceres de la sangre como leucemia mieloide aguda, leucemia mieloide crónica, etc, esófago de Barrett (síndrome pre- maligno), enfermedad neoplásica cutánea, psoriasis, micosis fungoides e hipertrofia prostática benigna, enfermedades relacionadas con diabetes tales como retinopatía diabética, isquemia retinal y neovascularización retinal, cirrosis hepática, enfermedad cardiovascular tal como ateroesclerosis, enfermedad inmunológica tal como enfermedad autoinmune y enfermedad renal. Preferiblemente, la enfermedad es cáncer tal como leucemia mieloide aguda y cáncer colorectal.

Ejemplos adicionales, sin limitación de los tipos de trastornos relacionados con actividad PK inapropiada que los compuestos descritos en la presente pueden prevenir, tratar y estudiar, son los trastornos de proliferación celular, trastornos fibróticos, trastornos metabólicos, y enfermedades infecciosas.

Los trastornos de proliferación celular que se pueden prevenir, tratar o estudiar adicionalmente mediante el presente invento incluyen cáncer, trastornos de proliferación

de vasos sanguíneos y trastornos de proliferación de células mesangiales.

Los trastornos de proliferación de vasos sanguíneos se refieren a trastornos relacionados con vasculogenesis anormal (formación de vasos sanguíneos) y angiogenesis (diseminación de vasos sanguíneos). Mientras la vasculogenesis y angiogenesis juegan papeles importantes en una variedad de procesos fisiológicos normales tales como desarrollo embriónico, formación del cuerpo lúteo, curación de heridas y regeneración de órganos, éstas también juegan un papel principal en el desarrollo del cáncer donde resultan en la formación de nuevas capilaridades necesarias para mantener un tumor vivo. Otros ejemplos de trastornos de proliferación de vasos sanguíneos incluyen artritis, donde nuevos vasos sanguíneos capilares invaden la articulación y destruyen el cartílago, y enfermedades oftálmicas, como la retinopatía diabética, donde nuevas capilaridades en la retina invaden el vítreo, sangran y producen ceguera.

La vasculogenesis y angiogenesis normales juegan papeles importantes en una variedad de procesos fisiológicos tales como desarrollo embriónico, curación de heridas, regeneración de órganos y procesos reproductivos femeninos tales como desarrollo de folículos en el cuerpo lúteo durante ovulación y crecimiento placentario después del embarazo. Folkman &Shing, 1992, J. Biological Chem., 267(16): 10931- 34. Vasculogenesis y/o angiogenesis no controladas han sido asociadas con enfermedades tales como diabetes así como también con tumores sólidos malignos que dependen de la vascularización para su crecimiento. Klagsburn & Soker, 1993, Current Biology, 3(10): 699- 702; Folkham, 1991, J. Natl. Cancer Inst., 82:4- 6; Weider, 1991, New Engl. J. Med., 324:1- 5

Como se entiende actualmente, el papel VEGF en migración y proliferación de células endoteliales durante angiogenesis y vasculogenesis indica un papel importante para el receptor KDR/FLK- 1 en estos procesos. Enfermedades tales como la diabetes mellitus (Folkman, 198, en XI Congreso de Trombosis y Haemostasis (Verstracta,), pp. 583- 596, Leuven University Press, Leuven) y artritis, así como también crecimiento turmoral maligno pueden resultar a partir de angiogenesis no controlada. Ver ej., Folkman, 1971, N. Engl. J. Med., 285:1182- 1186. Los receptores a los cuales VEGF específicamente se une son un objetivo terapéutico poderoso para la regulación y modulación de vasculogenesis y/o angiogenesis y una variedad de enfermedades severas las cuales involucran crecimiento celular anormal causado por tales procesos. Plowman, 1994, DN&P, 7(6):334- 339. Más particularmente, el papel altamente específico del

receptor KDR/FLK en neovascularización hacen de éste un blanco de elección para aproximaciones terapéuticas para el tratamiento del cáncer y otras enfermedades que pueden involucrar la formación incontrolada de vasos sanguíneos.

Por lo tanto, un aspecto del presente invento se relaciona con compuestos capaces de regular y/o modular transducción de señales de tirosinaquinasa incluyendo transducción de señales del receptor KDR/FLK con el objeto de inhibir o promover angiogenesis y/o vasculogenesis, es decir, compuestos que inhiben, previenen, o interfieren con la señal transducida mediante KDR/FLK- 1 cuando se activan mediante ligandos tales como VEGF. Aunque se cree los compuestos del presente invento actuan como un receptor u otro componente a lo largo de la ruta de transducción de señales de la tirosinaquinasa, éstos también pueden actuar directamente sobre las células tumorales que resultan a partir de angiogenesis no controlada.

Por lo tanto, en un aspecto, el presente invento está dirigido a compuestos que regulan, modulan y/o inhiben la vasculogenesis y/o angiogenesis al afectar la actividad enzimática del receptor KDR/FLK- 1 y al intervenir con la señal transducida por KDR/FLK- 1. En otro aspecto, el presente invento está dirigido a compuestos que regulan, modulan y/o inhiben la ruta de transducción de señales mediada por KDR/FLK- 1 como un enfoque terapéutico para el tratamiento de muchas clases de tumores sólidos incluyendo, pero sin limitar a, glioblastoma, melanona y sarcoma de Kaposi, y carcinoma ovárico, pulmonar, mamario, prostático, pancreático, de colon y epidermoide. además, los datos indican la administración de compuestos que inhiben la ruta de transducción de señales mediada por KDR/Flk- 1 se pueden utilizar en el tratamiento de hemangioma, restenosis y retinopatia diabética.

Un aspecto adicional de este invento se relaciona con la inhibición de vasculogenesis y angiogenesis mediante otras rutas mediadas por receptores, incluyendo la ruta que comprende el receptor fit- 1.

La traducción de señales mediadas por el receptor con actividad tirosinaquinasa es iniciada mediante interacción extracelular con un factor de crecimiento específico (ligando), seguido por la dimerización de receptores, estimulación temporal de la actividad intrínseca de la tirosina proteinaquinasa y autofosforilación. Los sitios de unión son creados de esta manera para moléculas de transducción de señales intracelulares lo cual lleva a la formación de complejos con un espectro de moléculas de señalización citoplásmica que facilita la respuesta celular apropiada, ej., división celular y efectos metabólicos al microambiente extracelular. Ver, Schlessinger y Ullrich, 1992,

Neuron, 9:1- 20.

La homología próxima de las regiones intracelulares de KDR/FLK- 1 con el receptor PDGF- □ (homología de 50.3%) y/o el receptor relacionado indica la inducción de rutas de transducción de señales superpuestas. Por ejemplo, para el receptor PDGF- □, los miembros de la familia src (Twamley, 1993, Proc. Natl. acad. Sci. USA, 90:7696- 7700), fosfatidilinositol- 3'- quinasa (Hu, 1992, Mol. Cell. Biol., 12:981- 990), fosfolipasa c□ (Kashinshian & Cooper, 1993, Mol. Cell. Biol., 4:49- 51), proteina activadora de la ras- GTPasa, (Kashishian, 1992, EMBO J., 11:1373- 1382), PTP- ID/syp (Kazlauskas, 1993, Proc. Natl. Acad. Sci. USA, 10 90:6939- 6943), Grb2 (Arvidsson, 1994, Mol. Cell. Biol. 14:6715- 6726), y las moleculas adaptadoras Shc y Nck (Nishimura, 1993, Mol. Cell. Biol., 13:6889- 6896), han sido mostrados uniendose a regiones que involucran diferentes sitios de autofosforilación. Ver generalmente, Claesson- Welsh, 1994, Prog. Growth Factor Res., 5:37- 54. Por lo tanto, es probable que las rutas de transducción de señales activadas mediante KDR/FLK- 1 incluyan la ruta ras (Rozakis, 1992, Nature, 360:689- 692), la PI- 3'- quinasa, las rutas mediadas por src y mediadas por plc□. Cada una de estas rutas puede jugar un papel crítico en el efecto angiogénico y/o vasculogénico de KDR/FLK- 1 en células endoteliales. Consecuentemente, un aspecto aún adicional de este invento se relaciona con el uso de compuestos orgánicos descritos en la presente para modular angiogenesis y vasculogenesis tal que los procesos son controlados por estas rutas.

A la inversa, los trastornos relacionados con el encogimiento, contracción o cierre de vasos sanguíneos, tal como restenosis, también están implicados y pueden ser tratados o prevenidos mediante los métodos de este invento.

Los trastornos fibróticos se refieren a la formación anormal de matrices extracelulares. Ejemplos de trastornos fibróticos incluyen cirrosis hepática y trastornos de proliferación de células mesangiales. La cirrosis hepática se caracteriza por el aumento en constituyentes de matriz extracelular que resultan en la formación de una cicatriz hepática. Una matriz extracelular aumentada que resulta en una cicatriz hepática también puede ser causada por una infección viral tal como la hepatitis. Los linfocitos parecen jugar un papel principal en la cirrosis hepática. Otros trastornos fibróticos implicados incluyen aterosclerosis.

Los trastornos de proliferación de células mesangiales se refieren a trastornos producidos por la proliferación anormal de células mesangiales. Los trastornos proliferativos mesangiales incluyen varias enfermedades renales humanas tales como

glomerulonefritis, nefropatía diabética y nefrosclerosis maligna así como también desórdenes tales como síndromes de microangiopatía trombótica, rechazo de transplantes, y glomerulopatias. El PDGFR de RTK ha sido implicado en el mantenimiento de proliferación de células mesangiales. Floege., 1993, Kidney International 43: 47S- 54S.

Muchos cánceres son trastornos de proliferación celular y, como se anotó anteriormente, las PKs han sido asociadas con trastornos de proliferación de células. Por lo tanto, no es sorprendente que las PKs tales como, por ejemplo, loa miembros de la familia RTK hayan sido asociadas con el desarrollo de cáncer. Algunos de estos receptores, como EGFR (Tuzi, 1991, Br. J. Cancer 63:227- 233, Torp, 1992, APMIS 100:713- 719) HER2/neU (Slamon, 1989, science 244:707- 712) y PDGF- R (Kumabe, 1992, Oncogene, 7:627- 633) son sobre- expresados en muchos tumores y/o persistentemente activados por bucles de autocrina. En realidad, en la mayoria de cánceres comunes y severos estas sobreexpresiones de los receptores (Akbasak y Suner-Akbasak, 1992, J. Neurol. Sci., 111:119- 133, Dickson, 1992, Cancer Treatment Res. 61: 249- 273, Korc, 1992, J. Clin. Invest. 90:1352- 1360) y blucles de autocrina (Lee and Donoghue, 1992, J. Cell. Biol., 118:1057- 1070, Korc., supra, Akbasak y Suner-Akbasak, supra) han sido demostradas. Por ejemplo, EGFR se ha asociado con carcinoma celular escamoso, astrocitoma, glioblastoma, cáncer de cabeza y cuello, cáncer pulmonar y cáncer de vejiga. HER2 se ha asociado con cáncer de mama, ovario, pulmón, páncreas, vejiga y cáncer gástrico. PDGFR se ha asociado con glioblastoma y melanoma así como también con cáncer pulmonar, ovárico y prostático. El c- met de RTK también se ha asociado con formación tumoral maligna. Por ejemplo, c- met se ha asociado con, entre otros cánceres, con carcinomas y linfomas colorectal, tiroideo, pancreático, gástrico y hepatocelular. Adicionalmente c.met se ha ligado a la leucemia. La sobrepresión del gen c- met también se ha detectado en pacientes con enfermedad de Hodgking y enfermedad de Burkitts.

IGF- IR, además de estar implicado en el soporte nutricional y en diabetes tipo II, también se ha asociado con diferentes tipos de cánceres. Por ejemplo, IGF- I ha sido implicado como un estimulador de crecimiento autócrino para varios tipos de tumores, ej., células de carcinomatosas de cáncer de mama humano (Arteaga, 1989, J. Clin. Invest.84:1418- 1423) y células pequeñas de de tumor pulmonar (Macauley 1990, Cancer Res., 50:2511- 2517). Además, mientras IGF- I se ha involucrado integralmente en el crecimiento normal y diferenciación del sistema nervioso, también parece ser un

simulador de autocrina en gliomas humanos. Sandberg- Nordqvist, 1993, Cancer Res. 53:2475- 2478. La importancia de IGF- IR y sus ligandos en proliferación celular es soportada adicionalmente por el hecho que muchos tipos celulares en cultivo (fibroblastos, células epiteliales, células de músculo liso, linfocitos- T, células mieloides, condrocitos y osteoclastos (las células madre de la médula ósea)) son estimulados a crecer por IGF- I. Goldring y Goldring, 1991, Expresión de Genes Eucarióticos, 1:301- 326. Baserga y Coppola señalan que IGF- IR juega un papel central en el mecanismo de transformación y, como tal, podría ser un blanco preferido para intervenciones terapéuticas para un espectro amplio de malignidades humanas. Baserga, 1995, Cancer Res., 55:249- 252, Baserga, 1994, Cell 79:927- 930, Coppola, 1994, Mol. Cell. Biol., 14:4588- 4595.

Las STKs han sido implicadas en muchos tipos de cáncer incluyendo, notablemente, cáncer de mama (Cancer, Int. J. Cancer, 54:571- 77 (1993)).

La asociación entre actividad PK anormal y enfermedad no está restringida al cáncer. Por ejemplo, las RTKs se han asociado con enfermedades tales como psoriasis, diabetes mellitus, endometriosis, angiogenesis, desarrollo de placa ateromatosa, enfermedad de Alzheimer, enfermedad de von Hippel- Lindau, hiperproliferación epidermal, enfermedades neurodegenerativas, degeneración macular relacionada con la edad y hemangiomas. Por ejemplo EGFR se ha indicado en curación de heridas corneas y dérmicas. Los defectos en Insulina- R y IGF- 1R son indicados en diabetes mellitus tipo- II. Una correlación más completa entre RTKs específicas y sus indicaciones terapéuticas es divulgada en Plowman, 1994, DN&P 7:334- 339.

Como se anotó anteriormente, no solamente las RTKs sino las CTKs incluyendo, pero sin limitar a src, abl, fps, yes, fyn, lyn, lck, blk, hck, fgr, y yrk (reseñadas por Bolen, 1992, FASEB J., 6:3403- 3409) están involucradas en la ruta de traducción de señales proliferativas y metabólicas y por lo tanto se podría esperar, y se ha demostrado, que están involucradas en muchos trastornos mediados por PTK a los cuales el presente invento está dirigido. Por ejemplo, scr (v- src) mutado ha sido mostrado como una oncoproteína ($pp60^{v\text{-}src}$) en pollos. Además, su homólogo celular, el prooncogeno pp60 c- arc transmite señales oncogénicas de muchos receptores. La sobre- expresión de EGFR o HER2/neu en tumores lleva a la activación constitutiva de $pp60^{c\text{-}src}$, lo cual es característica de células malignas pero ausente en células normales. Por otra parte, los ratones deficientes en la expresión de c.src exhiben un fenotipo osteopetrótico, indicando una participación clave de c- src en función de osteoclastos y una posible

relación con estos trastornos.

De manera similar, Zap70 ha sido implicado en la señalización de células- T lo cual se puede relacionar con trastornos autoinmunes.

Las STKs han sido asociadas con inflamación, enfermedad autoinmune, inmunorespuestas, y trastornos de hiperproliferación tales como restenosis, fibrosis, psoriasis, osteoartritis y artritis reumatoide.

Las PKs también han sido implicadas en implantación de embriones. Por lo tanto, los compuestos de esta invento pueden proporcionar un método efectivo para prevenir tal implantación de embriones y de esta manera ser útil como agentes de control natal.

En aún otro aspecto, los compuestos del presente invento también se pueden utilizar como agentes anti- infecciosos.

Finalmente, actualmente se sospecha que tanto las RTKs como las CTKs están involucradas en transtornos hiperinmunes.

Composiciones Farmaceuticas y Uso

Un compuesto del presente invento o sal farmacéuticamente aceptable del mismo, se puede administrar como tal a un paciente humano o se pueden administrar en composiciones farmacéuticas en los cuales estos materiales son mezclados con vehículos o excipientes apropiados. Las técnicas para la formulación y administración de fármacos pueden ser encontradas en "Ciencias Farmacológicas de Remington," Mack Publishing Co., Easton, PA., última edition.

Rutas de Administración

Las rutas apropiadas de administración pueden incluir, sin limitación, administración oral, rectal, transmucosal o intestinal o inyecciones intramusculares, subcutáneas, intramedulares, intratecales, intraventriculares directas, intravenosas, intravítreas, intraperitoneales, intranasales, o intraoculares. Las rutas preferidas de administración son orales o parenterales.

Alternativamente, el compuesto se puede administrar de una manera local más que sistémica, por ejemplo, a través de inyección del compuesto directamente en un tumor sólido, a menudo en un depósito o formulación de liberación sostenida.

Además, el fármaco se puede administrar en un sistema de liberación de fármaco dirigido, por ejemplo, en un liposoma recubierto con anticuerpo específico al tumor.

Los liposomas serán señalados y absorbidos selectivamente por el tumor.

Composición/Formulación

Las composiciones farmacéuticas del presente invento se pueden fabricar mediante procesos bien conocidos en el estado de la técnica, ejemplo, por medio de procesos de mezclado convencional, disolución, granulación, levigación, emulsificación, encapsulación, producción con aire ocluido, liofilización o secado por atomización.

Las composiciones farmacéuticas para utilizar en los métodos del presente invento se pueden preparar mediante cualquier método de farmacia, pero todos los métodos incluyen el paso de llevar en asociación el ingrediente activo con el vehiculo que constituye uno o más ingredientes necesarios. En particular, las composiciones farmacéuticas para utilizar según el presente invento se pueden formular en forma convencional utilizando uno o más vehiculos fisiológicamente aceptables que comprenden excipientes y auxiliares que facilitan el procesamiento de los compuestos activos en las preparaciones que se pueden utilizar farmacéuticamente. La formulación adecuada depende de la ruta de administración elegida.

Las formas de dosificación incluyen tabletas, grageas, dispersiones, suspensiones, soluciones, cápsulas, parches, jarabes, elixires, geles, polvos, magmas, pastillas, ungüentos, cremas, pastas, emplastos, lociones, discos, supositorios, atomizaciones nasales u orales, acrosoles y similares.

Para inyección, los compuestos del invento se pueden formular en soluciones acuosas, preferiblemente en amortiguadores fisiológicamente compatibles, tales amortiguadores con o sin una baja concentración de surfactante o cosolvente, amortiguador salino fisiológico. Para administración transmucosal, se utilizan penetrantes apropiados para la barrera a ser permeada en la formulación. Tales penetrantes son generalmente conocidos en el estado de la técnica.

Para administración oral, los compuestos se pueden formular combinando los compuestos activos con vehículos farmacéuticamente aceptables bien conocidos en el estado de la técnica. Tales vehículos permiten que los compuestos del invento sean formulados como tabletas, píldoras, pastillas, grageas, cápsulas, líquidos, geles, jarabes, suspensiones y similares, para ingestión oral por parte del paciente. Las preparaciones farmacéuticas para uso oral se pueden fabricar utilizando un excipiente sólido, opcionalmente triturando la mezcla resultante, y procesando la mezcla de granulos,

después de agregar otros aditivos apropiados si se desea, para obtener tabletas o núcleos de grageas. Excipientes útiles son, en particular, rellenos tales como azúcares, incluyendo lactosa, sacarosa, manitol, o sorbitan, preparaciones de celulosa tales como, por ejemplo, almidón de maíz, almidón de cebada, almidón de arroz y almidón de patata y otros materiales tales como gelatina, goma tragacanto, metilcelulosa, hidroxipropilmetilcelulosa, carboximetilcelulosa de sodio, y/o polivinilpirrolidona (PVP). Si se desea, se pueden agregar agentes desintegrantes, tales como polivinilpirrolidona entrecruzada, agar, o ácido algínico. También se puede utilizar una sal tal como alginato de sodio.

Los núcleos de grageas son proporcionados con recubrimientos apropiados. Para este propósito, se pueden utilizar soluciones concentradas de azucar las cuales opcionalmente pueden contener goma arábiga, talco, polivinilpirrolidona, gel carbopol, glicol de polietileno, y/o dióxido de titanio, soluciones de laca y solventes orgánicos apropiados o mezclas solventes. Se pueden agregar colorantes o pigmentos a las tabletas o recubrimientos de grageas para identificación, para caracterizar diferentes combinaciones de dosis de compuestos activos.

Las composiciones farmacéuticas que se pueden utilizar oralmente incluyen cápsulas tipo *push-fit* hechas de gelatina, así como también cápsulas suaves selladas hechas de gelatina y un plastificante, tal como glicerol o sorbitol. Las cápsulas tipo *push-fit* pueden contener los ingredientes activos en mezcla con un relleno tal como lactosa, un aglomerante tal como almidón, y/o un lubricante tal como talco o estearato de magnesio y, opcionalmente, estabilizadores. En cápsulas suaves, los compuestos activos se pueden disolver o suspender en líquidos apropiados, tal como aceites grasos, parafina líquida, o glicoles de polietileno líquido. También se pueden agregar estabilizantes en estas formulaciones.

Para administración mediante inhalación, los compuestos para utilizar según el presente invento son convenientemente liberados en la forma de una atomización de aerosol utilizando una paca presurizada o un nebulizador y un propulsor adecuado ej., sin limitación, diclorodifluorometano, triclorofluorometano, diclorotetrafluoroetano o dióxido de carbono. En el caso de un aerosol presurizado, la unidad de dosificación puede ser controlada proporcionando una válvula para liberar una cantidad medida. Las cápsulas y cartuchos de, por ejemplo, gelatina para utilizar en un inhalador o insuflador pueden ser formuladas conteniendo una mezcla en polvo del compuesto y una base de polvo apropiada tal como lactosa o almidón.

Los compuestos también se pueden formular para administración parenteral, ejemplo, mediante inyección de bolo o infusión continua. Las formulaciones para inyección se pueden presentar en forma de dosificación unitaria, ejemplo, en ampollas o en recipientes de múltiples dosis, con un preservativo agregado. Las composiciones pueden tener formas tales como suspensiones, soluciones o emulsiones en vehículos aceitosos o acuosos, y pueden contener materiales de formulación tales como agentes de suspensión, estabilización y/o dispersión.

Las composiciones farmacéuticas para administración parenteral incluyen soluciones acuosas de una forma soluble en agua, tal como, sin limitación, una sal del compuesto activo. Adicionalmente, se pueden preparar suspensiones de los compuestos activos en un vehículo lipofílico. Vehículos lipofílicos apropiados incluyen aceites grasos tales como aceite de ajonjolí, ésteres de ácidos grasos sintéticos tales como oleato de etilo y triglicéridos, o materiales tales como liposomas. Las suspensiones de inyección acuosa pueden contener sustancias que aumentan la viscosidad de la suspensión, tal como carboximetilcelulosa de sodio, sorbitol, o dextran. Opcionalmente, la suspensión también puede contener estabilizantes apropiados y/o agentes que aumentan la solubilidad de los compuestos para considerar la preparación de soluciones altamente concentradas.

Alternativamente, el ingrediente activo puede estar en forma de polvo para constitución con un vehículo apropiado, ejemplo, estearilo, agua libre de pirogenos, antes de utilizar.

Los compuestos también se pueden formular en composiciones rectales tales como supositorios o enemas de retención, utilizando, ej., bases supositorias convencionales tales como manteca de cacao u otros triglicéridos.

Además de las formulaciones previamente descritas, los compuestos también se pueden formular como preparaciones depot. Tales formulaciones de acción prolongada pueden ser administradas mediante implantación (por ejemplo, subcutanea o intramuscular) o mediante inyección intramuscular. Un compuesto de este invento puede ser formulado para esta ruta de administración con materiales poliméricos o hidrofóbicos apropiados (por ejemplo, en una emulsión con un aceite farmacologicamente aceptable), con resinas de intercambio iónico, o como un derivado apenas soluble tal como, sin limitación, una sal apenas soluble.

Alternativamente, otros sistemas de liberación para compuestos farmacéuticos hidrofóbicos pueden ser empleados. Los liposomas y emulsiones son ejemplos bien

conocidos de vehículos de liberación para fármacos hidrofóbicos. Además, ciertos solventes orgánicos tales como dimetilsulfoxido también pueden ser empleados, aunque a menudo con un costo de gran toxicidad.

Adicionalmente, los compuestos se pueden liberar utilizando un sistema de liberación sostenida, tal como matices semipermeables de polímeros hidrofóbicos sólidos que contienen el agente terapéutico. Se han establecido varios materiales de liberación sostenida y son bien conocidos por aquellos con experiencia en el estado de la técnica. Las cápsulas de liberación sostenida pueden, dependiendo de su naturaleza química, liberar los compuestos durante un periodo entre pocas semanas y más de 100 días. Dependiendo de la naturaleza química y la estabilidad biológica del reactivo terapéutico, se pueden emplear estrategias para estabilización de proteínas.

Las composiciones farmacéuticas en la presente también pueden comprender vehículos o excipientes apropiados de fase sólida o gelatinosa. Ejemplos de tales vehículos o excipientes incluyen, pero no están limitados a carbonato de calcio, fosfato de calcio, varios azúcares, almidones, derivados de celulosa, gelatina, y polímeros tales como glicoles de polietileno.

Muchos de los compuestos moduladores de PK del invento pueden ser proporcionados como sales fisiológicamente aceptables en donde el compuesto reivindicado puede formar las especies con carga negativa o positiva. Ejemplos de sales en las cuales el compuesto forma la fracción de carga positiva incluyen, sin limitación, sales de amonio cuaternarias tales como hidrocloruro, sulfato, carbonato, lactato, tartrato, malato, maleato, succinato en donde el átomo de nitrógeno del grupo de amonio cuaternario es un nitrógeno del compuesto seleccionado de este invento el cual ha reaccionado con el ácido apropiado. La sales en las cuales un compuesto de este invento forma la especie con carga negativa incluyen, sin limitación, sales de potasio de sodio, calcio y magnesio formadas mediante la reacción de un grupo ácido carboxílico en el compuesto con una base apropiada (ejemplos hidroxido de sodio (NaOH), hidroxido potasio (KOH), hidroxido de calcio ($Ca(OH)_2$), etc).

Dosificación

Las composiciones farmacéuticas apropiadas para utilizar en el presente invento incluyen composiciones en donde los ingredientes activos son contenidos en una cantidad suficiente para lograr el propósito deseado, ej., la modulación de la actividad PK o el tratamiento o prevención de un trastorno relacionado con PK.

Más específicamente, una cantidad terapéuticamente efectiva significa una cantidad de un compuesto efectivo para prevenir, aliviar o mejorar síntomas de una enfermedad o prolongar la expectativa de vida del sujeto tratado.

La determinación de una cantidad terapéuticamente efectiva está dentro de la capacidad de aquellos con experiencia en el estado de técnica, especialmente a la luz de la divulgación detallada proporcionada en la presente.

Para cualquier compuesto utilizado en los métodos del invento, la cantidad o dosis terapéuticamente efectiva puede ser estimada inicialmente a partir de ensayos de cultivos celulares. Luego, la dosis puede ser formulada para utilizar en modelos animales para así lograr un rango de concentración circulante que incluye el IC50 tal como se determina en cultivo celular (es decir, la concentración del compuesto de prueba que logra una inhibición media- máxima de la actividad PK). Tal información luego puede ser utilizada para determinar con mayor exactitud las dosis útiles en humanos.

La toxicidad y eficacia terapéutica de los compuestos descritos en la presente pueden ser determinadas mediante procedimientos farmacéuticos estándares en cultivos celulares o animales experimentales, ej. mediante la determinación de IC50 y LD50 para un compuesto bajo examen. Los datos obtenidos a partir de estos ensayos de cultivos celulares y estudios animales se pueden utilizar para formular un rango de dosificación para utilizar en humanos. La dosificación puede variar dependiendo de la forma de dosificación empleada y la ruta de administración utilizado. La formulación, ruta de administración y dosis pueden ser elegidas por un médico en vista de la condición del paciente. (Ver ej., Fingl, 1975, "The Pharmacological Basis of Therapeutics", Ch. 1 p.1).

La cantidad de dosificación e intervalo se pueden ajustar individualmente para proporcionar niveles de plasma de las especies activas que son suficientes para mantener efectos de modulación de la quinasa. Éstos niveles de plasma son conocidos como concentraciones efectivas mínimas (MECs). La MEC variará para cada compuesto pero se puede estimar a partir de datos in vitro, ej., la concentración necesaria para lograr una inhibición 50- 90% de una quinasa se puede indagar utilizando ensayos descritos en la presente. Las dosificaciones necesarias para lograr MEC dependerán de las características individuales y la ruta de administración. Los ensayos HPLC o bioensayos se pueden utilizar para determinar concentraciones de plasma.

Los intervalos de dosificación también se pueden determinar utilizando el valor

MEC. Los compuestos se deben administrar utilizando un régimen que mantenga los niveles de plasma por encima de MEC durante 10- 90% del tiempo, preferiblemente entre 30- 90% y lo más preferiblemente entre 50- 90%. Actualmente, las cantidades terapéuticamente efectivas de los compuestos inventivos descritos en la presente pueden estar en el rango entre aproximadamente 25 mg/m^2 y 1000 mg/m^2 por día. Aún más preferiblemente entre 25mg/m^2 y 150mg/m^2.

En casos de administración local o absorción selectiva, la concentración local efectiva del fármaco puede no estar relacionada con la concentración de plasma, y otros procedimientos conocidos en el estado de la técnica se pueden emplear para determinar la cantidad de dosificación e intervalo correctos.

La cantidad de una composición administrada, naturalmente, dependerá del sujeto tratado, la severidad de la aflicción, la forma de administración, el juicio del médico, etc.

Las composiciones, si se desea, se pueden presentar en un empaque o dispositivo dispensador, tal como un kit aprobado por la FDA, el cual puede contener una o más formas de dosificación unitarias que contienen el ingrediente activo. El empaque por ejemplo puede comprender papel metálico o plástico, como por ejemplo un empaque blister. El empaque o dispositivo dispensador puede estar acompañado por instrucciones para administración. El empaque o dispensador también puede estar acompañado por un aviso asociado con el recipiente en una forma prescrita por una agencia gubernamental que regula la fabricación, uso o venta de farmacos, tal aviso refleja la aprobación por parte de la agencia de la forma de las composiciones o de administración veterinaria o humana. Tal aviso, por ejemplo, puede ser de la rotulación aprobada por la Administración Americana de Alimentos y Fármacos para prescripción de fármacos o de un inserto de producto aprobado. Composiciones que comprenden un compuesto del invento formulado en un vehículo farmacéutico compatible también pueden ser preparadas, colocadas en un recipiente apropiado, y rotulados para tratamiento de una condición indicada. Condiciones apropiadas indicadas en el rótulo pueden incluir el tratamiento de un tumor, inhibición de angiogenesis, tratamiento de fibrosis, diabetes, y similares.

EJEMPLOS

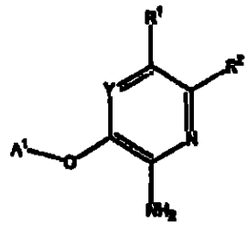
Los siguientes ejemplos son dados para ilustrar el presente invento. Sin embargo, se debe entender que el invento no está limitado a las condiciones específicas

o detalles descritos en estos ejemplos.

La numeración en los ejemplos corresponde a la numeración en las tables en la presente. Los esquemas de reacción y numeros de ejemplos que comienzan con una letra (I) se relacionan con compuestos de piridina, mientras aquellos que comienzan con una letra (II) se relacionan con compuestos de pirazina. Los números de ejemplo que comienzan con L son síntesis de bibliotéca. Los números de ejemplo con una notación de letra (a, b, c, etc) ilustran la síntesis de reactivos subsecuentemente utilizados en la síntesis de los compuestos inventivos, los cuales tienen una notación numérica (1, 2, 3, etc.). Los reactivos se pueden sintetizar como se muestra en la presente, o están disponibles a partir de fuentes comerciales (ej., Aldrich, Milwaukee, WI; Acros, Morris Plains, NJ; Biosynth Unternational, Naperville, IL; Frontier scientific, Logan, UT; TCI America, Portland, OR; Combi- Blocks, San Diego, CA; Matrix Scientific, Columbia, SC; Acros, Morris Plains, NJ; Alfa Aesar, Ward Hill, MA; Apollo Scientific, UK; etc.) o se pueden sintetizar mediante procedimientos conocidos en el estado de la técnica. Cuando se cita un procedimiento sintético general o de ejemplo, alguien con experiencia en el estado de la técnica facilmente puede determinar los reactivos apropiados, si estos no se indican, extrapolando a partir de los procedimientos generales o de ejemplo.

En los procedimientos generales 1- 43 descritos en la presente, aunque algunos de los procedimientos son generalizados y de ejemplo, el tiempo pasado se utiliza para indicar que estos procedimientos generales fueron los procedimientos utilizados para sintetizar los compuestos. Algunos de los procedimientos generales son dados como ejemplos para preparar los compuestos específicos. Alguien con habilidad en el estado de la técnica puede facilmente adaptar tales procedimientos a la síntesis de otros compuestos. Se debe entender que los grupos R mostrados en los procedimientos generales son genéricos y no limitantes, y no corresponden a definiciones de grupos R en otra parte en este documento. Cada grupo R representa una o múltiples fracciones químicas que pueden ser iguales o diferentes de otras fracciones químicas también representadas por el mismo símbolo R. Además, la representación de una posición no substituida en las estructuras mostradas o citadas en los procedimientos generales es por conveniencia y no evita sustitución tal como se describe en otra parte en la presente. Para grupos específicos que se pueden representar, ya sea como grupos R en los procedimientos generales o como sustituyentes opcionales no mostrados, se refiere a las descripciones en el resto de este documento, incluyendo las reivindicaciones, resumen y descripción detallada. Se debe entender además que los números de compuestos

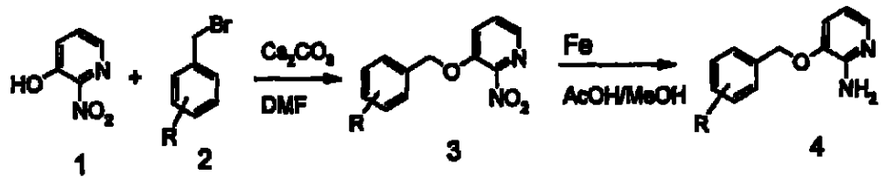
mostrados en los esquemas general y procedimientos generales en los Ejemplos son solamente para referencia conveniente, y no corresponden a los numeros utilizados en otra parte en este documento. Por ejemplo, el compuesto de nitropiridina (1) en el esquema general I es diferente del compuesto de la formula 1 descrito en la presente.

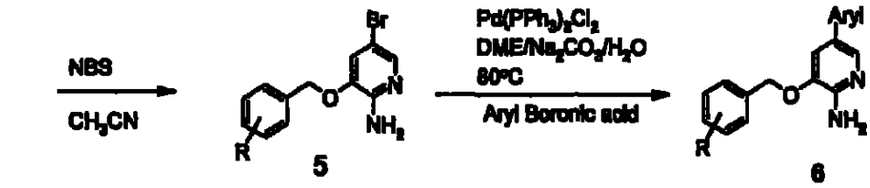


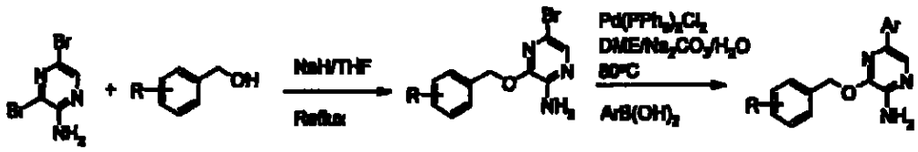
1

Esquema General I para la síntesis de 5- aril- 3- (benciloxilo sustituido)- piridin- 2- ilamina (6):

Esquema General II para la síntesis de 5- aril- 3- (benciloxilo sustituido)- pirazin- 2- ilamina







Procedimiento General 1 para la síntesis de 5- bromo- 3- (benciloxilo sustituido)- piridin- 2- ilamina (5):

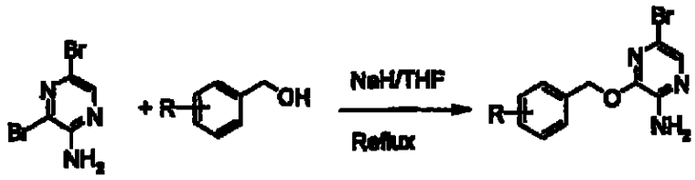
1.Preparación de 3- (benciloxilo substituido)- 2- nitro- piridina (3): A una solución agitada de Cs2CO3 (1.0 molar equivalente) en DMF (0.2 M) bajo una atmósfera N2 conteniendo 3- hidroxi- 4- nitro- piridina (Aldrich, 1.0 molar equivalente) se agrego bromuro de bencilo substituido (1.0 molar equivalente). La mezcla fue agitada durante 6 horas a temperatura ambiente. Luego la reacción fue diluida con EtOAc, y particionada con H2O. La capa acuosa fue extraída dos veces con EtOAc. Luego las capas orgánicas fueron combinadas, lavadas con H2O y salmuera, secadas sobre

Na2SO4, filtradas y concentradas hasta sequedad al vacío para proporcionar 3- (benciloxilo substituido)- 2- nitro- piridina (3) como un sólido.

2. Preparación de 3- (benciloxilo substituido)- piridin- 2- ilamina (4): A una mezcla agitada de AcOH y EtOH (1.3:1) se suspendió 3- (benciloxi- 2- nitro- piridina substituida) (1.0 molar equivalente, 1 M) y trozos de hierro (1.0 molar equivalente). La reacción fue sometida lentamente hasta reflujo y dejada agitar durante una hora. La reacción fue enfriada a temperatura ambiente luego filtrada a través de un cojín de Celite. El filtrado resultante fue neutralizado con NH4OH concentrado, y luego se extrajo con EtOAc durante tres veces. Luego los extractos orgánicos combinados fueron lavados con NaHCO3 saturado, H2O, y salmuera secados sobre Na2SO4, filtrados y concentrados hasta sequedad al vacío para proporcionar 3- (benciloxilo substituido)- piridin- 2- ilamina (4) como un sólido.

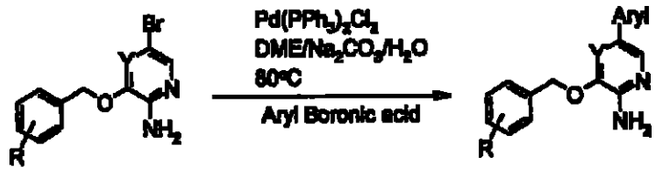
3. preparación de 5- bromo- 3- (benciloxilo substituido)- piridin- 2- ilamina (5): una solución agitada de 3- (benciloxilo substituido)- piridin- 2- ilamina (4) (1.0 molar equivalente) en acetonitrilo fue enfriada 0 °C utilizando un baño de hielo. A esta solución se agregó N- bromosuccinimida (aldrich, 1.0 molar equivalente) por porciones. La reacción fue agitada a 0 °C durante 15 minutos. La reacción fue concentrada hasta sequedad al vacío. El aceite oscuro resultante fue disuelto en EtOAc y particionado con H2O. Luego la capa orgánica fue lavada dos veces con NaHCO3 saturado y una vez con salmuera. Se agregó carbón de leña activado a la capa orgánica y se calentó hasta reflujo. Luego la solución fue enfriada a temperatura ambiente y filtrada a través de un cojín de Celite. Luego la capa orgánica fue concentrada hasta sequedad al vacío hasta un tercio del volumen original. Luego los sólidos fueron filtrados para proporcionar 5- bromo- 3- (benciloxilo substituido)- pirazin- 2- ilamina (5) como un sólido.

Procedimiento general 2 para la síntesis de 5- bromo- 3- (benciloxilo substituido)- pirazin- 2- ilam



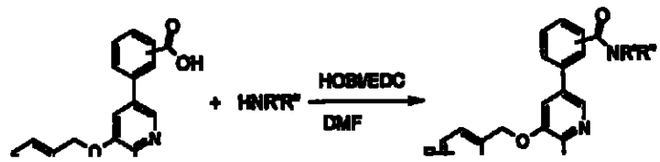
A una solución fría de alcohol bencilico substituido (1.0 molar equivalente) y tetrahidrofurano anhidro se agregó hidruro de sodio (1.0 molar equivalente) lentamente bajo atmósfera de nitrógeno. Después de agitar durante 30 minutos, 3,5-dibromopirazin- 2- ilamina (1.0 molar equivalente) en tetrahidrofurano (0.56 M) se agregó a través de un embudo de adición a una tasa rápida de goteo. Una vez terminada la adición el baño de hielo fue retirado y la reacción fue sometida a reflujo bajo nitrógeno y monitoreada mediante HPLC de fase inversa. Después de 18 horas HPLC mostró que la mayoría de 3,5- dibromopirazin- 2- ilamina de inicio había sido consumida y la reacción fue dejada enfriar a temperatura ambiente. La mezcla de reacción fue concentrada, diluida con acetato de etilo, y lavada con salmuera. La capa orgánica fue secada sobre sulfato de magnesio anhidro y concentrada al vacío. El producto crudo fue purificado utilizando gel de sílice eluyendo con 1:1acetato/diclorometano etilico para proporcionar la 5- bromo- 3- (benciloxilo substituido)- pirazin- 2- ilamina como un sólido blanco en rendimiento de 60- 90%.

Procedimiento general 3 para la síntesis de 5- aril- 3- (benciloxilo substituido)- piridin- 2- ilamina y 5- aril- 3- (benciloxilo substituido)- pirazin- 2- ilamina.



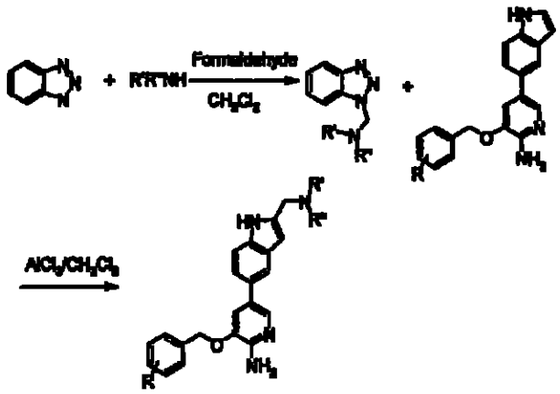
Una mezcla de 5- bromo- 3- (benciloxilo substituido)- piridin- 2- ilamina o 5- bromo- 3- (benciloxilo substituido)- pirazin- 2- ilamina (1 molar equivalente), ácido boronico de arilo o éster (1,2 molar equivalente), cloruro de bis(trifenilfosfina) paladium II (0.03molar equivalente) y carbonato de sodio (3.0 molar equivalente) en eter dimetilico de glicol de etileno y agua (10:o.5, 0.03 M) fue degasificada y cargada con nitrógeno tres veces, y luego calentada a reflujo bajo nitrógeno durante la noche. La reacción fue enfriada a temperatura ambiente y diluida con acetato de etilo. La mezcla fue lavada con agua, salmuera, secada sobre Na2SO4, y purificada sobre una columna de gel de sílice para proporcionar 5- aril- 3- (benciloxilo substituido)- piridin- 2- ilamina o 5- aril- 3- (benciloxilo substituido)- pirazin- 2- ilamina.

Procedimiento general 4 para reacción de amidación del ácido 6- amino- 5- (benciloxilo substituido)- piridin- 3- il]- benzoico:



A una solución de ácido 6- amino- 5- (benciloxilo substituido)- piridin- 3- il]- benzoico (1 molar equivalente), hidrato de 1- hidroxibenzotriazol (HOBT, 1.2 molar equivalente), y hidrocloruro de 1- (3- dimetilaminopropil)- 3- etilcarbodiimida (EDC, 1.2 molar equivalente) en DMF (0.2 M) se agregó amina (1.2 molar equivalente). La solución de reacción fue agitada a temperatura ambiente durante la noche, luego diluida con EtOAc, y particionada con H2O. La capa orgánica fue separada y la capa acuosa fue extraída con EtOAc. Las capas orgánicas fueron combinadas, lavadas con NaHCO3 saturado y concentradas hasta sequedad al vacío. El material fue purificado utilizando cromatografía de columna (gel de sílice, 99:1 a 95:5 CH2Cl2/MeOH). Las fracciones que contiene el producto fueron concentradas al vacío para proporcionar el producto amida.

Producto general 5 para la preparación de 3- (benciloxilo substituido)- 5- (3- dialkilaminometil- 1H- indol- 5- il)- piridin- 2- ilamina:

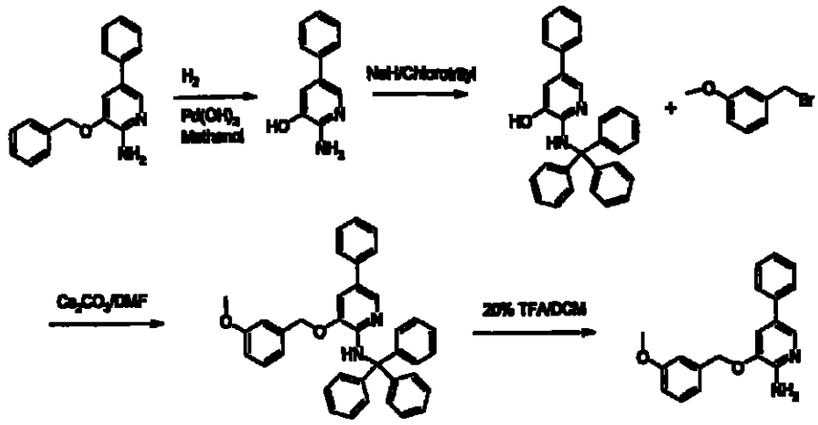


A una solución de benzotriazol (1.0 molar equivalente) en diclorometano (0.2 M) se agregó amina (1.0 molar equivalente). La reacción fue agitada durante 5 minutos a temperatura ambiente, después de lo cual se agregó formaldehido (37% por Wt, 1.0 molar equivalente) y la reacción fue tapada y agitada a temperatura ambiente durante 3 horas. Una vez TLC (10% acetato de etilo: diclorometano) mostró el consumo de

bencotriazol de inicio, la reacción fue secada con sulfato de magnesio anhidro (10g), filtrada y concentrada al vacío. El producto crudo fue purificado con una columna de gel de sílice eluyendo con 1:1 acetato de etilo: diclorometano para proporcionar el producto deseado como un sólido blanco.

A una solución del compuesto intermedio de aminometilbenzotriazol (1.0 molar equivalente) en diclorometano (0.43 M) se agregó cloruro de aluminio (2.0 molar equivalente) y luego seguido por (2,6- dicloro- benciloxi)- 5- (1H- indol- 5- il)- piridina- 2- ilamin (1.1 molar equivalente). La reacción fue tapada calentada con agitación de 40 °C durante 3- 4 horas. Luego la reacción fue removida del calor y dejada enfriar a temperatura ambiente. La mezcla de reacción fue diluida con hidroxido de sodio (0.2M) y cloroformo, tapada nuevamente y agitada vigorosamente a temperatura ambiente para disolver el residuo en la matraz. El cloroformo fue extraído de la capa acuosa, secado sobre sulfato de sodio anhidro y concentrado al vacío. El producto crudo fue purificado con una columna de gel de sílice, eluyendo primero con 1:1, acetato de etilo: diclorometano, para eluir las impurezas menos polares y luego eluyendo el producto con) 90:9:1, cloroformo: metanol:hidroxido de amonio. (rendimientos 10- 67%)

Procedimiento general 6 para síntesis de 3- (benciloxilo substituido)- 5- fenil- piridin- 2- ilamina utilizando el ejemplo I- 88



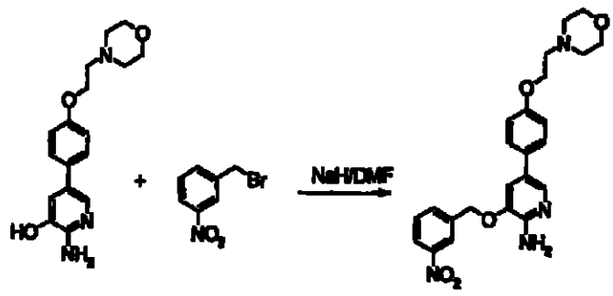
A una solución de 3- benciloxi- 5- fenil- piridin- 2- ilamina (Ejemplo I- 87, 3.27g, 11.8mmol) en metanol (30mL) se agregó Pd (OH)2 (2.5g, 2.37 mmol). La mezcla fue degasificada y cargada con hidrogeno tres veces, y luego agitada bajo un globo de hidrogeno durante 5 horas. La reacción fue filtrada a través de un cojín de

Celite, lavada con metanol, y condensada. Después de secar a alto vacío, se obtuvo 2- amino- 5- fenil- piridin- 3- ol (2.04g, rendimiento 93%). MS m/z187 [M+1].

A una solución de 2- amino- 5- fenil- piridin- 3- ol (2.04 g, 10.95 mmol) en THF (anhidro, 30 mL) se agregó NaH (1.31 g, 32.85 mmol) lentamente. La mezcla fue agitada bajo nitrogeno durante 20 minutos, y luego se agregó cloruro de tritilo (3.66g, 13.14 mmol). La reacción fue agitada a temperatura ambiente durante la noche bajo nitrógeno. El solvente fue evaporado, y el residuo fue disuelto en diclorometano, lavado con agua, y secado sobre Na2SO4. Después filtrado y condensado, el producto crudo fue purificado sobre una columna de gel de sílice eluyendo con EtOAc- hexano (1:10) para proporcionar 5- fenil- 2- (tritil- amino)- piridin- 3- ol (1.09 g, rendimiento 23%). MS m/z 427 [M+1].

A una solución de 5- fenil- 2- (tritil- amino)- pirridin- 3- ol (100 mg, 0.24 mmol) in THF (3 mL) se agregó Cs2CO3 (79 mg, 0.24 mmol). La mezcla fue agitada a temperatura ambiente durante 20 minutos, y luego se agregó 3- metoxibencilbromuro (0.037 mL, 0.26 mmol). La reacción fue agitada a temperatura ambiente durante la noche, diluida con diclorometano (5 mL), y filtrada para remover las sales. Los solventes fueron evaporados, y el residuo fue disuelto en ácido trifluoroacetico al 10% en diclorometano (2 mL). La reacción fue agitada durante 2 horas, y evaporada . el residuo fue disuelto en diclorometano, lavado con NaHCO3 saturado, y secado sobre Na2SO4 después filtrado y concentrado, el producto crudo fue purificado sobre una columna de gel sílice eluyendo con metanol- diclorometano (gradiente de 3% a 15%) para proporcionar 3- (3- metoxi- benciloxi)- 5- fenil- piridin- 2- ilamina como un sólido blanco (43.5 mg, rendimiento 60%).

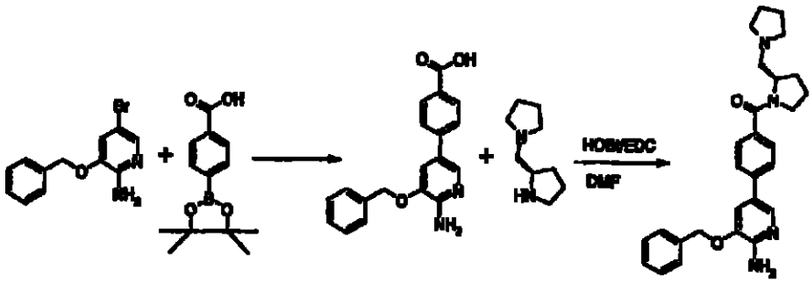
Procedimiento general 7 para la síntesis de 3- (benciloxilo substituido)- 5- aril- piridin- 2- ilamina utilizando el ejemplo I- 106:

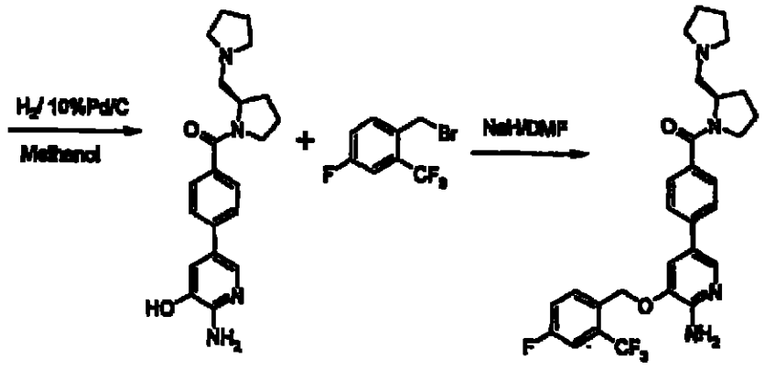


A una solución de 2- amino- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 3- ol (preparado según los procedimientos para 2- amino- 5- fenil- piridin- 3- ol en el

Ejemplo I- 88) (45.5 mg, 0.14 mmol) en DMF (3 mL) a 0 °C se agregó NaH (60% en aceite) (5.6 mg, 0.14 mmol) y la mezcla fue agitada a 0 °C durante 20 minutos. Luego se agregó 1- bromometil- 3- nitro- benceno y la mezcla fue agitada a 0 °C durante 1 hora y a temperatura ambiente durante 2 horas. Se agregó HCl acuoso 1 N frío (0.1 mL) y el solvente fue removido bajo presión reducida. El residuo fue purificado con cromatografía de gel de sílice (CH2Cl2:MeOH: NH4OH = 100: 3:0.3) para proporcionar 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- 3- (3- nitro- benciloxi)- piridin- 2- ilamina como un sólido amarillo (44 mg, 68%).

Procedimiento general 8 para la síntesis de {4- [6- amino- 5- (benciloxilo substituido)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona utilizando el ejemplo I- 111:





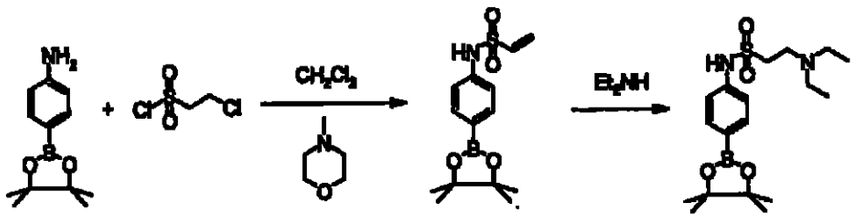
El ácido 6- amino- 5- benciloxi- nicotinico fue preparado según el procedimiento 3 a partir de 3- benciloxi- 5- bromo- piridin- 2- ilamina y ácido 4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- benzoico.

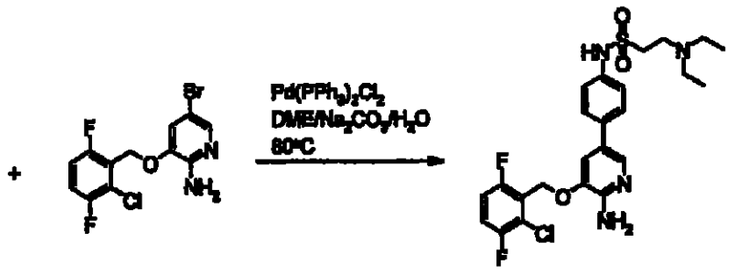
[4- (6- amino- 5- benciloxi- piridin- 3- il)- fenil]- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona fue preparada siguiendo el procedimiento 4 utilizando ácido 6- amino- 5- benciloxi- nicotinico y (2R)- pirrolidin- 1- ilmetil- pirrolidina (preparada en el Ejemplo I- 39). MS 457 (M+1).

A una solución de [4- (6- amino- 5- benciloxi- piridin- 3- il)- fenil]- [(2R)- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona (2.28 g, 5.00 mmol) en metanol (25 mL) se agregó Pd/C (100 mg) al 10%. La mezcla fue degasificada y cargada tres veces con hidrogeno y luego se agito bajo un globo de hidrogeno durante la noche. La reacción fue filtrada a través de un cojín de Celite, lavada con metanol, y condensada. Después de secar a alto vacío, se obtuvo [4- (6- amino- 5- hidroxi- piridin- 3- il)- fenil]- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona (1.74 g, rendimiento 95%). ^{1}H NMR(400 MHz, DMSO- d6) δ 7.79 (s, 1H), 7.54 (m, 3H), 7.46 (m, 2H), 7.14(s, 1H), 5.68 (s, 2H), 4.22(m, 1H), 3.45 (m, 2H), 2.66 (m, 1H), 2.52 (m, 4H), 1.96 (m, 2H), 1.84 (m, 3H), 1.64 (m, 4H); MS m/z367 (M+1).

A una solución agitada de [4- (6- amino- 5- hidroxi- piridin- 3- il)- fenil]- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona (100 mg, 0.27 mmol) en DMF anhidro (15 mL) bajo una atmósfera de N2, a 0 °C, se agregó hidruro de sodio (dispersión de 60% en aceite mineral, 11mg, 0.49 mmol). La mezcla se agito a 0 °C durante 30 minutos. Se agregó 1- (bromometil)- 4- fluoro- 2- (trifluorometil)- benzeno (0.046 mL, 0.27 mmol). La mezcla fue agitada a temperatura ambiente durante 2 horas. La reacción fue diluida con EtOAc, y particionada con H2O. La capa acuosa fue extraída con EtOAc (2 x 25 mL). Las capas orgánicas fueron combinadas, lavadas con H2O (1 x 15 mL), salmuera (1 x 15mL), secadas sobre MgSO4, filtradas, concentradas, y purificadas sobre una columna de gel de sílice para proporcionar {4- [6- amino- 5- (4- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona como cristales blancuzcos.

Procedimiento general 9 para la síntesis de [6- amino- 5- (benciloxilo substituido) del ácido 2- diakilamino- etanosulfónico utilizando el Ejemplo I- 243.





A una solución de 4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenilamida (5 g, 22.8 mmol) en diclorometano (120 mL) se agregó morfolina de N- metilo (7.5 mL, 68.4 mmol). Esta mezcla fue enfriada a 0 °C bajo atmósfera de nitrógeno. Luego se agregó por goteo cloruro de 2- cloroetanosulfonilo (2.5 mL, 23.9 mmol) en diclorometano (60 mL) con agitación. Una vez terminada la adición la matraz fue agitada a 0 °C durante 1 hora y luego a temperatura ambiente mientras se realiza monitoreo por TLC (1:1 acetato de etilo:hexanos) y decoloración con ninhidrina. Después de agitar durante 4 horas algún ester boronico de inicio aún permanecio y un equivalente 0.2 adicional (0.5 mL) de cloruro de 2- cloroetanosulfonilo en diclorometano (25 mL) se agregó por goteo a temperatura ambiente. Después de 1 hora el ester borónico se consumió como se muestra mediante TLC y el volumen total de reacción fue reducido en la mitad a través de evaporación rotatoria. Los contenidos fueron diluidos con acetato de etilo (200 mL), lavados con salmuera (2 x 100 mL) al 50% secados sobre sulfato de sodio anhidro y concentrados al vacío. El producto crudo fue purificado utilizando gel de sílice (120g) y eluyendo con acetato de etilo al 10%, diclorometano para proporcionar [4- (4,4,55- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido etanosulfónico como un sólido blanco (6.2 g, 20.2 mmol, rendimiento 89%) ^{1}H NMR(CDCl3, 300 MHz) δ 7.76 (d, J=8.4, 2H), 7.12 (d, J=8.45 2H), 6.65 (s, 1H), 6.55 (dd, J=9.77, 6.7, 1H), 6.31 (d, J=16.54, 1H), 5.96 (d, J=9.8, 1H), 1.33 (s, 12H).

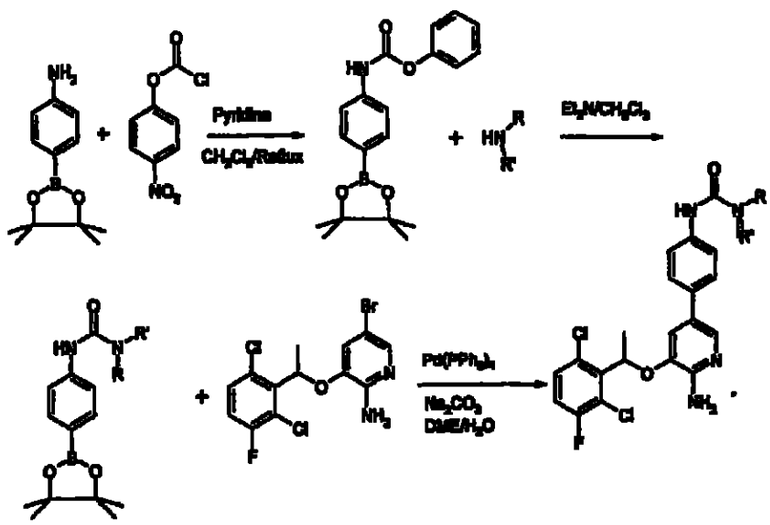
2. A una solución [4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido etanosulfónico se agregó dietilamina 80.707 g, 4.0 mmol) en metanol (5 mL), la reacción fue agitada a temperatura ambiente y monitoreada mediante TLC (1:1 acetato de etilo: hexanos). Después de 2 horas la reacción fue concentrada al vacío y el residuo particionado entre acetato de etilo (50 mL) y agua (50 mL). Luego el acetato de etilo fue lavado con salmuera (1 x 50 mL) al 50%, secado sobre sulfato de sodio anhidro, filtrado y concentrado al vacío. El producto crudo fue purificado utilizando una columna de gel de sílice pre- empacada de 10 g, eluyendo con 1:1 acetato de etilo: diclorometano para proporcionar [4,4,5,5- tetrametil- [1,3,2]dioxoborolan- 2- il)- fenil]- amida del ácido dietilamino- etanosulfónico como un solido. ^{1}H NMR (CDCl3, 300 MHz) δ 7.78 (d, J=6.65, 2H), 7.15 (d, J=6.66 2H), 3.0 (m, 2H), 2.55 (q, J=9.15, 7.16 4H), 1.34 (s, 12H), 1.05 (t, J=7.19, 6H).

3. {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- dietilamino- etanosulfónico siguiendo el procedimiento general 3 de acoplamiento Suzuki a partir de 5- bromo- 3- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 2- ilamina y [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- dietilamino- etanosulfónico preparada en la parte 2 como un sólido blanco en rendimiento de 60%.g

Procedimiento general 10

1: 4- (4,4,5,5- tetrametil 1,3,2 dioxaboralan- 2- il)anilina (3 g, 0.013 mol) fue disuelto en diclorometano (350 mL) a la cual se agregó piridina (1.02 g, 0.013 mol) y cloroformato de 4- nitrofenilo. La reacción fue agitada durante 13 horas donde el análisis TLC mostró cons

umo de todos los materiales de inicio. La solución fue lavada con NaHCO3 (3 x 50 mL) saturada, agua (3 x 50 mL) y salmuera (3 x 50 mL). La capa orgánica fue secada sobre Na2SO4 y el solvente removido para proporcionar un sólido cristalino blanco. Ester fenil del ácido [4- (,4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- carbamico, 4.45 g, 91%. ^{1}H NMR (CDCl3, 300 MHz) δ 1.4 (s, 12H), 7.1 (br, 1H), 7.3 (d, 2H), 7.5 (d, 2H), 7.8 (d, 2H), 8.3 (d, 2H).

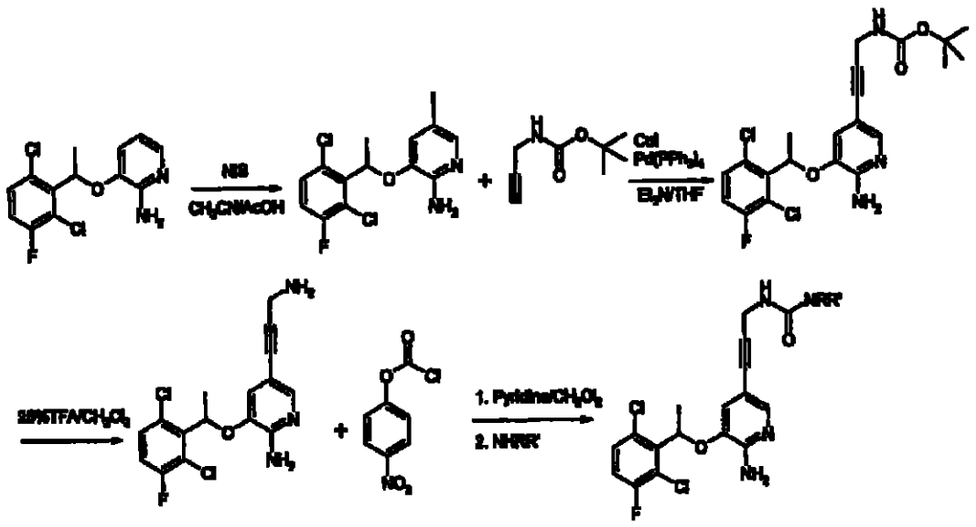


2. Ester fenilo del ácido [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- carbamico (500 mg, 1.3 mmol) fue disuelto en diclorometano anhidro (0.5 mL) y trietilamina (0.187 mL, 1.3 mmol). A esta solución agitada se agregó piperazina de 1-

metilo (o cualquier otra amina) (0.144 mL, 1.3 mmol). La solución se torno amarilla de manera inmediata, y el análisis de TLC mostró consumo de todos los materiales de inicio. La reacción fue lavada con agua (3 x 500 mL), bicarbonato de sodio saturado (2 x 200 mL) y secada antes de retirar los solventes al vacío. Los ésteres boronicos fueron utilizados sin purificación.

3. A una mezcla de 2.1 mL DME y 2.8 mL de Na2CO3 2N se agregó 100 de armazón de bromuro, 1 equivalente de el ácido boronico, y 5 mol % de Pd(pph3)4. La reacción fue agitada y calentada a 80 °C durante la noche en un frasco de dos dracmas. La mezcla cruda fue filtrada a través Celite y extraída con EtOAc (2 x 100 mL). Los extractos combinados fueron lavados con NaCO3 (1 x 100 mL), seguido por agua (1 x 100 mL), y luego salmuera saturada (1 x 100 mL). La mezcla resultante fue concentrada al vacio. El residuo fue disuelto en hexano y purificado a través de cromatografía de columna.

Procedimiento general 11



1: A una solución de 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina (10.0 g, 33.2 mmol) en acetonitrilo (600 mL) y ácido acetico (120 mL) se agregó N- iodosuccinimida (11.2 g, 49.8 mmol). La mezcla fue agitada a temperatura ambiente durante 4 horas. Y la reacción fue apagada con solución de Na2S2O5. Después evaporada, el residuo fue particionado entre acetato de etilo y agua. La capa

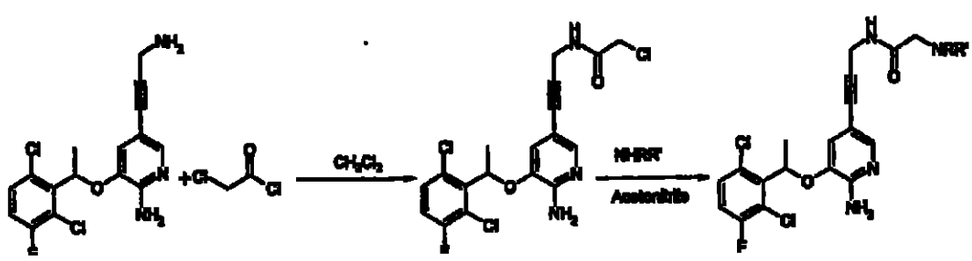
orgánica fue lavada con solución NaOH 2N, salmuera y secada sobre Na2SO4. El producto fue purificado sobre un gel de sílice para proporcionar 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- yodo- piridin- 2- ilamina (7.1 g rendimiento 50%).MS m/z 427 [M+1]

2: A una solución de 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- yodo- piridin- 2- ilamina (7.1 g, 16.6 mmol) y éster tert- butilo del ácido prop- 2- inil- carbamico (3.1 g, 20.0 mmol) en THF y Et3N (60 mL) se agregó CuI (63 mg, 0.3 mmol) y Pd(PPh3)4 (384 mg, 0.3 mmol). La mezcla fue agitada bajo nitrógeno y monitoreada mediante TLC hasta que se completo la reacción. La mezcla fue extraída con EtOAc y lavada mediante agua. El producto crudo fue purificado sobre una columna de gel de sílice eluyendo con 20- 40% de EtOAc en hexano para proporcionar éster tert- butilo del ácido (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- carbamico (2.2 g, rendimiento 29%).

3: La solución de éster tert- butilo del ácido (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- carbamico en 25% TFA en diclorometano fue agitada durante 2 horas, luego lavada mediante NaOH 2N, agua dos veces, salmuera, se seco sobre Na2SO4. Después de filtración y evaporación, se obtuvo 5- (3- amino- prop- 1- inil)- 3- [1- (2.6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina en rendimiento al 93%.

4: A una solución de 5- (3- amino- prop- 1- inil)- 3- [1- (2.6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina (0.282 mmol, 1. Eq) y cloroformato de 4- nitrofenilo (1 eq) en diclorometano anhidro (10 mL) se agregó piridina (1 eq). La reacción fue agitada durante 4 horas bajo nitrógeno, y luego se agregó la amina seleccionada (1 eq) y trietilamina (1 eq). La mezcla fue sometida a reflujo durante 5 minutos y enfriada a temperatura ambiente. La mezcla de reacción fue lavada con agua. La capa orgánica fue evaporada y purificada sobre una columna de gel de sílice eluyendo con o- 20% metanol en diclorometano sobre columnas de sílice pre- empacadas. Los rendimientos finales variaron entre 24% y 71%.

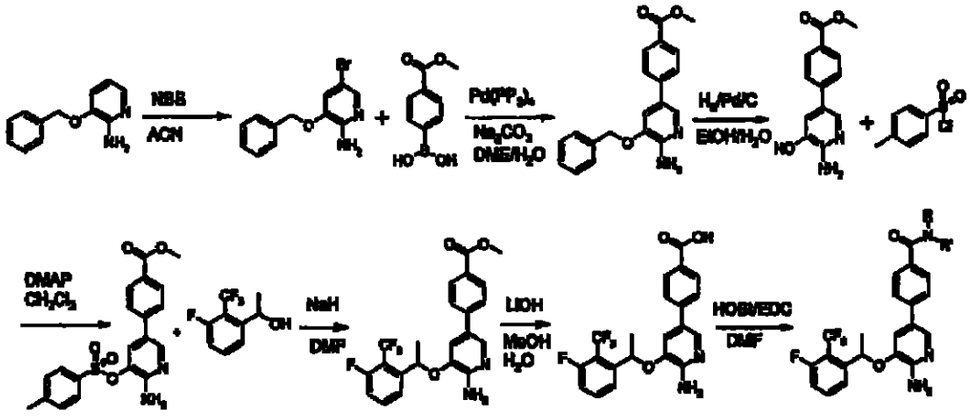
Procedimiento general 12:



1: A una solución de 5- (3- amino- prop- 1- inil)- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina (preparada en el procedimiento 11) (400 mg, 1.1 mmol) en diclorometano (17 mL) se agregó cloruro de cloroacetilo (153 mg, 1.4 mmol). La reacción fue agitada a temperatura ambiente, monitoreando mediante TLC la terminación de la reacción. Después de la terminación , el solvente fue evaporado para obtener el producto crudo.

2: A una solución de N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- cloro- acetamida (1 eq) en acetonitrilo (5 eq) se agregó la amina individual (5 eq). La mezcla fue sometida hasta reflujo bajo nitrógeno durante la noche. Después la evaporación del solvente, el residuo fue purificado sobre una columna de gel de sílice eluyendo con 1- 10% demetanol en diclorometano para proporcionar el producto. Los rendimientos finales variaron entre 47% a 97%.

Procedimiento general 13:



1. A una solución agitada de 2- amino- 3- benciloxipiridina (42.0 g, 0.21 mol) en CH3CN (600 mL) a 0 °C se agregó N- bromosuccinimida (37.1.g, 0.21 mol) durante 30 minutos. La mezcla fue agitada durante 0.5 horas, luego la reacción fue diluida con EtOAc (900 mL) y particionada con H2O (900 mL). la capa orgánica fue lavada con salmuera y secada con (Na2SO4), filtrada y concentrada hasta sequedad al vacío para proporcionar 3- benciloxi- 5- bromo- piridin- 2- ilamina (31.0 g, 0.11 mol, 53%). H^1

NMR (CDCl3, 300 MHz) δ 4.63- 4.78 (brs,2H), 5.04 (s, 2H), 7.07 (d, 1H, J, 1.8 Hz), 7.33- 7.42 (m, 5H), 7.73 (d, 1H, J, 1.8 Hz).

2. A una mezcla agitada de 3- benciloxi- 5- bromo- piridin- 2- ilamina (31.0 g, 0.11) en una mezcla de DME (600 mL) y H20 (600 mL) se agregó ácido 4- carboximetilboronico (29.9 g, 0.11 mol),Pd(PPh3)4 g, (6.4 5.55 mmol), y Na2CO3 (82.0 g, 0.78 mol). La reacción fue calentada hasta reflujo lentemente y dejada agitar durante 3 horas. La reacción fue enfriada a temperatura ambiente, luego diluida con CH2Cl2 (1.5 L) y particionada con H2O (700 mL). La capa organica fue lavada con NaHCO3 saturada (700 mL), secada con (Na2SO4), filtrada y concentrada al vacío. El material crudo fue purificado mediante cromatografía de columna (gel de sílice, 1:1 a 4:1 EtOAc:hexanos) y las fracciones que contienen el producto fueron combinadas y concentradas al vacío para proporcionar éster metilo del ácido 4- (6- amino- 5- benciloxi- piridin- 3- il)- benzoico (29.4 g, 0.86 mol, 79%). H^1 NMR (CDCl3, 300 MHz) δ 3.92 (s, 2H), 7.22 (d, 1H, J, 1.8 Hz), 7.33- 7 (m, 5 H), 7.54 (d, 2H, J, 8.6), 7.98 (d, 1H, J, 1.8 Hz), 8.06 (d, 2H, J, 8.6 Hz).

3. A una solución de éster metilo del ácido 4- (6- amino- 5- benciloxi- piridin- 3- il)- benzoico (10.0g, 0.03 mol) en EtOH:H2O (95:5, 600 mL) se agregó Pd/C (15.9 g; 0.015 mol) (la reacción fue degasificada al vacío). La solución se dejó agitar bajo una atmósfera de H2 durante 22 horas. La solución fue filtrada a travésde Celite humedo y el Celite lavado con EtOH. El filtrado fue concentrado al vacío para proporcionar éster metilo del ácido 4- (6- amino- 5- hidroxi- piridin- 3- il)- benzoico (2.3 g, 9.3 mmol,31%). H^1 NMR (MeOD, 300 MHz) δ 3.90 (s, 3H), 7.21 (d, 1H, J, 1.9 Hz), 7.62 (d, 2H, J. 8.5 Hz), 7.76 (d, 1H, J, 1.9 HZ), 8.04 (d, 2H, J, 8.5 Hz).

4. A una solución agitada de éster metilo del ácido 4- (6- amino- 5- hidroxi- piridin- 3- il)- benzoico (2.3 g, 9.3 mmol) en CH2Cl2 (180 mL) se agregó N,N- diisopropilotilamina (3.2 mL, 0.019 mol), cloruro de 4- metil- bencenosulfonil (2.66 g, 0.014 mol), y PS_DMAP (cantidad catalitica). La reacción fue agitada a temperatura ambiente durante 6 horas luego filtrada para remover la resina. La resina fue lavada con CH2Cl2 (3 x20 mL), y las fracciones combinadas fueron lavadas con ácido cítrico al 10% (100 mL), NaCl saturada (100 mL), secada sobre (Na2SO4), filtradas y concentradas al vacío. El material crudo resultante fue purificado mediante cromatografia de columna (gel de sílice, 100% CH2Cl2 a 95:5 CH2Cl2:MeOH) y las fracciones que contienen el producto deseado fueron combinadas y concentradas al

vacío para proporcionar éster metilo del ácido 4- [6- amino- 5- (tolueno- 4- sulfoniloxi)- piridin- 3- il]- benzoico. (3.3 g, 8.2 mmol, 88%). H^1 NMR (CDl3, 300 MHz) δ 2.47 (s, 3H), 2.93 (s, 3H), 4.81- 4.88 (brs, 2H), 7.36- 7.44 (m, 5H), 7.81 (d, 2H, J, 8.3 Hz). 8.05 (d, 2H, J, 8.4 Hz), 8.19- 8.27 (brs, 1H).

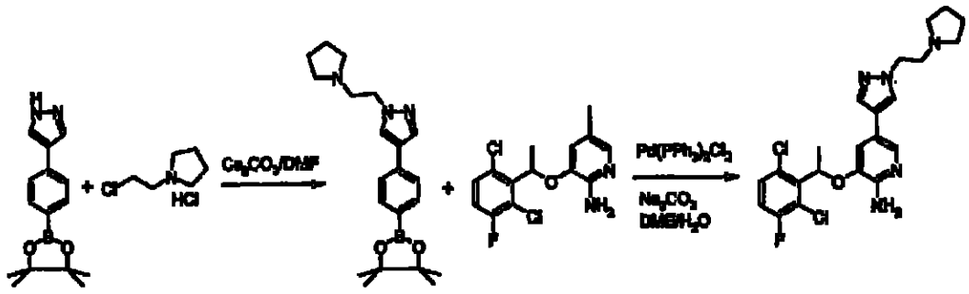
5. A una solución de 1- (3- fluoro- 2- trifluorometil- fenil)- etano (2.0 g, 9.6 mmol) en DMF (500 mL) a 0 ℃ bajo una atmósfera de N2 se gregó NaH (0.38 g, 9.6 mmol). La reacción se dejó agitar durante 0.5 horas. A una solución de éster metilo del ácido 4- {6- amino- 5- (toluoeno- 4- sulfoniloxi)- piridin- 3- il]- benzoico (3.8 g, 9.6 mmol) en DMF anhidro (30 mL) se agregó la mezcla de reacción la cual se dejo llegar hasta temperatura ambiente lentamente y se agito durante 21 horas a esta temperatura. La reacción fue diluida con EtOA (500ML) y H2O (100 mL). La capa orgánica fue separada y la capa acuosa fue extraída adicionalmente con EtOAc (1 x 200 mL). Las capas organicas fueron combinadas y lavadas con salmuera (1 x 100 mL), secadas con Na2SO4 y concentradas hasta sequedad al vacío. La mezcla cruda fue purificada mediante cromatografía en columna (gel de sílice, 40:60 a 70:30 EtOAc: hexanos) y las fracciones que contienen el producto fueron combinadas y concentradas al vacío para proporcionar éster metilo del ácido 4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- benzoico (1.4 g, 3.2 mmol). H^1 NMR (CDCl3, 300 MHz) δ 1.73 (d, 3H, J, 6.2 Hz), 3.91 (s, 3H), 4.87- 4.64 (brs, 2H), 8.51 (q, 1H, J, 6.1, 6.3 HZ), 6.92 (d, 1H, J, 1.8 Hz), 7.38 (d, 2H, J, 8.5 Hz), 7.46- 7.66 (m, 3H), 7.93 (d, 1H, J, 1.8 Hz), 8.02 (d, 2H, J, 8.5 Hz).

6. A una solución agita de éster metilo 4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- benzoico (1.4 g, 3.2 mmol) en IPA (72 mL) caliente se agregó H2O (38 mL) conteniendo LiOH (0.68 g, 26.2 mmol). La reacción fue calentada a reflujo durante 3.5 horas. La reacción fue neutralizada y diluida con EtOAc (200 mL) y extraida con enfriamiento. La capa orgánica fue lavada con salmuera (50 mL), y secada sobre Na2SO4 al vacío para proporcionar ácido 4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- benzoico (1.2 g, 2.8 mmol, 88%). H^1 NMR (MeOD, 300 MHz) δ 1.75 (d, 3H, J, 6.2, Hz), 4.88- 4.93 (m, 1H), 7.01 (d, 1H, J, 1.8 Hz), 7.52- 7.67 (m, 3H), 7.80 (d, 1H, J, 1.8 Hz), 7.97 (d, 2H, J, 8.3 Hz).

7. Preparación de los compuestos de amida: una solución agitada de ácido4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- benzoico (50 mg, 0.12 mmol), EDC (27.0 mg, 0.13 mmol) y HOBt (18.0 mg, 0.13 mmol) in DMF (2

mL) se agregó a un frasco de dos dracmas que contiene NHR1R2 (0. 12 mmol). La reacción fue agitada a temperatura ambiente durante 18 horas. Luego la reacción fue diluida con CH2Cl2 (3 mL) y particionada con H2O. La capa orgánica fue separada y lavada con NaCl saturado (1 x 2 mL) y NaHCo3 saturado (1 x 2 mL). La capa orgánica fue concentrada hasta sequedad al vacío. El material fue purificado utilizando cromatografía de columna (gel de sílice, 99:1 a 95:5 CH2Cl2/MeOH). Las fracciones que contienen el producto fueron concentradas al vacío para proporcionar los compuestos de amida.

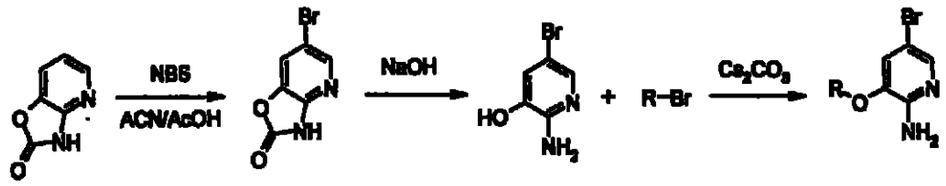
Procedimiento general 14



1: A una mezcla de hidrocloruro de 1- (2- cloroetil)pirrolidina (200 mg, 1.18 mmol) y 4- [4- (4,4,5,5- tetrametil- [1,3,2]dioxaboral- 2- il)- fenil]- 1H- pirazola (229 mg, 1.19 mmol) en DMF (6 mL) se agregó Cs2CO3. La mezcla fue agitada a temperatura ambiente durante la noche. Luego se agregó agua (10 mL) a la mezcla. El producto fue extraido con EtOAc (3 x 10 mL). Luego los extractos combinados fueron lavados con salmuera (5 x 10 mL) para remover el DMF, luego secados sobre Na2SO4 y concentrados (142 mg, rendimiento 41%).

2: A una mezcla de 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- yodo- piridin- 2- ilamina (200 mg, 0..468 mmol), éster pinacol- boronico (1.2 eq), Na2CO3 (149 mg,1.41 mmol) en agua (1.25 mL), y glicol etílico de dimetilo (3.75 mL, 0.1M) se agregó pd(PPh3)2Cl2 (16 mg, 0.020 mmol) en un recipiente de reacción de microondas. El sistema fue degasificado y cargado con nitrogeno. La mezcla fue agitada a 160 °C en un aparato de microondas durante 15 minutos. La mezcla fue enfriada a temperatura ambiente seguido por la adición de agua (10 mL). El producto fue extraído con EtOAc (3 x 20 mL), secada sobre Na2SO4, y concentrada. El producto crudo fue purificado mediante HPLC de fase inversa con 0.1% TFA en agua y acetonitrilo.

Procedimiento general 15

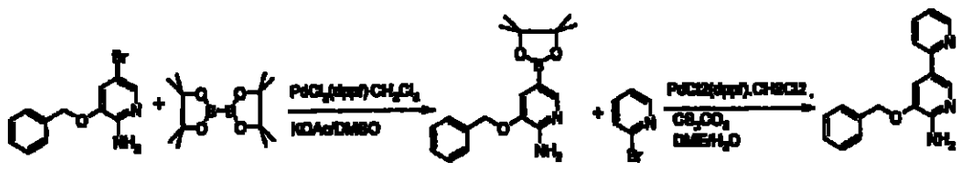


1: A una solución de 3H- oxazolo[4,5- b]piridin- 2- ona (13.6 g, 100 mmol) en acetonitrilo (600 mL) y ácido acetico (120 mL) se agregó N- bromosuccinimida (21.4 g, 120 mmol). La mezcla fue agitada a temperatura ambiente durante 4 horas y la reacción fue apagada con solución de Na2S2O5. Después de evaporación, el residuo fue particionado entre acetato de etilo. La capa orgánica fue lavada con solución NaOH 2N, salmuera, y seccada sobre NaSO4. El producto crudo fue purificado sobre una columna de gel de sílice para proporcionar 6- bromo- 3H- oxazolo[4,5- b]piridin- 2- ona (11. 5 g, rendimiento 55%).

2: 6- bromo- 3H- oxazolo[4,5- b]piridin- 2- ona (21.5 g, 100 mmol) fue suspendido en solución NaOH (2N, 250 mL, 500 mmol). La mezcla fue sometida a reflujo durante la noche y se obtuvo una solución clara. Después de enfriar a temperatura ambiente. La solución de reacción fue neutralizada a PH ~7. Se liberó mucho CO2 y también se observó un precipitado. El producto fue filtrado, lavado con agua, y secado al vacío para proporcionar 2- amino- 5- bromo- piridin- 3- ol como un sólido blancuzco (17.8 g; rendimiento 98%).

3: A una solución de 2- amino- 5- bromo- piridin- 3- ol (358 mg, 1.89 mmol) en DMF (8 mL) se agregó Cs2CO3 (620 mg, 1.89 mmol). La mezcla fue agitada a temperatura ambiente bajo nitrógeno durante 1 hora. A la mezcla de reacción se agregó compuesto de bromo (0.9 eq) en DMF (5 mL) lentamente. La solución de reacción fue agitada bajo nitrogeno durante cinco horas, y particionada entre agua y acetato de etilo. La capa orgánica fue lavada con salmuera tres veces, secada sobre MgSo4. El producto crudo fue purificado sobre una columna de gel de sílice eluyendo con acetato de hexano- etilo (4:1) para proporcionar producto con rendimiento del 70%- 80%.

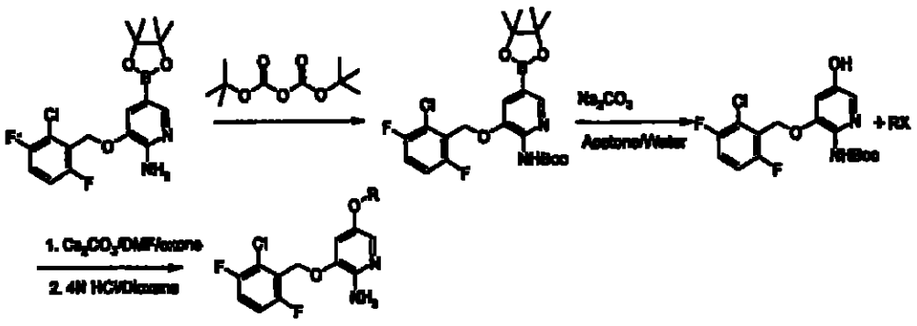
Procedimiento general 16 utilizando el Ejemplo I- 488:



1. A una solución de 3- benciloxi- 5- bromo- piridin- 2- ilamina (1 g, 3.58 mmol) en dimetilsulfoxida (7 mL) se agregó secuencialmente bis(pinacoloato)diborano (1.0 g, 3.94 mmol), acetato de potasio (1.05 g, 10.7 mmol)[1,1'-bis(difenilfosfino)ferrocina]dicloropaladio (II), complejo con diclorometano (1:1) (146 mg, 0.18 mmol). La mezcla fue calentada a 80°C durante 16 horas y luego enfriada a temperatura ambiente. La mezcla de reacción fue diluida con acetato de etilo (50 mL) y filtrada. El filtrado fue lavado con agua (2x50 mL) y secado sobre sulfato de magnesio. La concentración al vacío proporciono el boronato crudo como un sólido marrón. H^1 NMR (CDCl3) δ 1.32 (s, 12H), 5.08 (s, 2H), 5.44 (brs, 2H), 7.33- 7.42 (m, 6H).

2. Un recipiente de reacción fue cargado con 3- benciloxi- 5- (4,4,5,5- tetrametil-[1,3,2]dioxaborolan- 2- il)- piridin- 2- ilamina cruda (161 mg,0.49 mmol), dimetoxietano 83 mL) y 2- bromopiridina (117 mg, 0.74 mmol). A esta solución se agregó [1,1'- bis(difenilfosfino)ferrocina]dicloropaladio (II), complejo con diclorometano (1:1) (20 mg, 0.05 mmol) y en una solución de 2M de carbonato de celsio en agua (0.75 mL, 1.5 mmol). El reactor fue calentado a 80 °C durante 66 horas bajo una atmósfera de nitrógeno, luego enfriado a temperatura ambiente. Lamezcla de reacción fue particionada entre acetato de etilo (5 mL) y agua (5 mL). L a capa orgánica fue lavada con agua adicional (5 mL) y diluido con dimetilformamida (5 mL). Se agregó ácido sulfónico unido a polímeros (0.5 g, 2.1 mmol) a la solución orgánica, y la mezcla resultante fue agitada suavemente durante 2 horas. La resina fue filtrada y lavada con dimetilformamida, metanol y cloruro de metileno (3 x 5 mL cada solvente). Luego el polímero se hizo reaccionar con amoniaco 2M en metanol durante 1 hora. La resina fue filtrada y lavada amoniaco 2M adicional en metanol (2x5 mL), y los filtrados combinados fueron concentrados al vacío. La purificación del producto crudo mediante cromatografia de columna rapida proporcionó 52.2 mg del producto como un sólido de color canela.

Procedimiento general 17

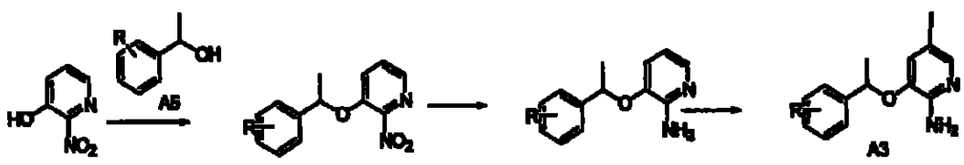


1. A la solución de 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- piridin- 2- ilamina (procedimiento 16) (10.0 g, 24.3 mmol) en alcohol de t- butilo (50 mL) se agregó anhidro boc (5.83 g, 26.7 mmol) y la reacción se agito a temperatura ambiente durante la noche. Se agrego adicionalmente anhidro boc (2.25 g, 10.3 mmol) y la reacción se agitó durante la noche nuevamente. El material fue concentrado en un aceite negro viscoso y utilizado como tal.

2. El éster boromico crudo (24.3 mmol teórico) en THF (150 mL) se agregó a una solución de bicarbonato de sodio (16.3 g, 194 mmol) en agua (150 mL) y acetona (23 mL). La mezcla fue enfriada a 2 °C y se agregó lentamente oxono (13.5 g, 21.9 mmol), manteniendo la temperatura bajo 8 °C. al terminar la adición la reacción fue agitada durante 5 minutos luego apagada con bisulfuro de sodio (14.2 g) en agua (28 mL). Se agregó acetato de etilo (200 mL) y las capas fueron separadas. La capa acuosa fue neutralizada con HCl 6N y extraída con acetato de etilo (2 x 200 mL). Las capas orgánicas combinadas fueron lavadas con agua (250 mL) y salmuera (250 mL), secadas sobre (NaSOr) y a un aceite negro crudo. La cromatografía de gel de sílice (acetato de etilo/hexano) proporciono el producto como una espuma de color marrón claro (4.78 g, 49.0%). H^1 NMR (CDCl3) δ 1.48 (s, 9H), 1.74 (d, 3H), 5.75 (q, 1H), 6.61 (d, 1H), 76.89 (dt, 1H), 6.94- 7.04 (m, 2H), 7.26 (d, 1H), 8.19 (bs, 1H). MS m/z 401 $(M+H)^+$.

3. A carbonato de cesio en un frasco de dos dracmas se agregó éster tert- butilo del ácido [3- (2- cloro- 3,6- difluoro- benciloxi)- 5- hidroxi- piriidn- 2- il}- carbamico (100 mg, 0.25 mmol) en DMF anhidro (1 mL) seguido por bromuro de bencilo (89 µL, 0.75 mmol). La matraz fue tapada y agitada a 90 °C durante la noche. La reacción fue filtrada a través de un tubo Chem- Elut de 5 mL pre- humedecía con agua n(3.5 mL) y eluida con 1:1 acetato de etilo: cloruro de metileno. Después parcialmente concentrado, se agregó HCl 4N en dioxono (1- 2 mL) y la solución se concentrada. La cromatografía de fase inversa (agua: acetonitrilo, 0.05% TFA) seguida por liofilización, proporcionó el producto deseado como un sólido amorfo de color blanco (25.3 mg, 20.0%) y el producto de doble adición como un sólido amorfo de color canela (35.2 mg, 23.7%).

Procedimiento general 18:



Se agregó borohidruro de sodio (1.5 molar equivalente) a una solución de cetona (3.89 mmol) en 10 mL de etanol bajo una atmósfera de nitrógeno. La mezcla resultante fue agitada a temperatura ambiente durante 12 horas. Luego la mezcla fue colocada en un baño de hielo y apagada con HCl acuoso diluido. el etanol fue evaporado y se agregó EtOAc para extraer la solución acuosa. La capa de EtOAc fue secada sobre Na2SO4, el Na2SO4 fue filtrado, y el filtrado fue evaporado para proporcionar un residuo aceitoso, compuesto A5. El residuo fue utilizado sin purificación adicional.

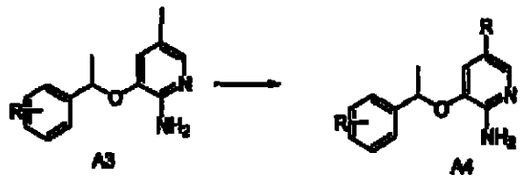
3- hidroxi- 2- nitropiridina (1:1 molar equivalente) y trifenilfosfina (1.5 molar equivalente) fueron agregados a una solución del compuesto A5 (1.1 mmol) en 10 mL de THF. Luego la mezcla de reacción fue puesta en un baño de hielo y se agregó azodicarboxilato de diisopropilo (1.5 molar equivalente). El baño de hielo fue removido y la mezcla fue agitada a temperatura ambiente durante 12 horas. El solvente fue evaporado para proporcionar un residuo aceitoso amarillo. El residuo fue purificado por cromatografía de gel de sílice (eluyendo EtOAc en hexanos) para proporcionar el compuesto A1.

Se agregó HCl 2M (0.2 mL) a una solución del compuesto A1 (0.97 mmol) en 2 mL de etanol. Luego la mezcla fue colocada en un baño de hielo y se agregó polvo de Fe (365 mg) lentamente. La reacción fue calentada a 85 °C durante 1 hora y enfriada a temperatura ambiente. Se agregó Celite (0.5 g) para agitar y la mezcla resultante fue filtrada a través de un lecho de Celite y enjuagada con etanol. El filtrado fue evaporado para proporcionar un residuo aceitoso de color marrón, compuesto A2. El residuo fue usado sin purificación adicional.

Se agregó ácido peryódico (0.25 molar equivalente) , yodo (0.5 molar equivalente), H2O (0.5 mL) y ácido sulfúrico concentrado (0.03 mL) a una solución del compuesto A2 en 3 mL de ácido acético. La mezcla de reacción fue calentada a 85 °C durante 5 horas. Luego la mezcla de reacción fue enfriada en un baño de hielo y basificada con Na2CO3 acuoso saturado a un pH de 3- 4. Se agregó acetato de etilo para extraer la solución acuosa. La capa de EtOAc fue secada sobre Na2SO4. El Na2So4 fue filtrado y el filtrado fue evaporado para proporcionar un residuo aceitoso de color

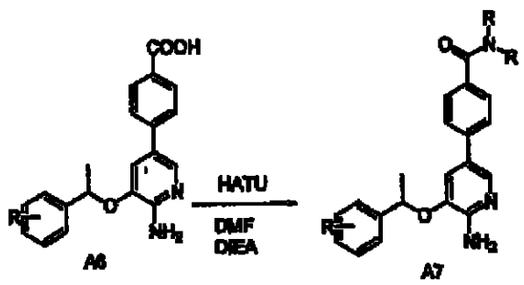
marron el residuo fue purificado por cromatografía de gel de sílice (eluyendo con EtOAc y hexanos) para proporcionar el producto deseado, compuesto A3.

Procedimiento general 19:



Se agregó éster borónico o ácido borónico (1.3 molar equivalente) a una solución del compuesto A3 (0.47 mmol) en 5 mL de DMF. La mezcla fue purgada con nitrógeno varias veces y luego se agregó diclorobis(trifenilfosfino)paladio (II) (0.05 molar equivalente). Se agregó carbonato de sodio (3 molar equivalente) en 1mL de H2O a la mezcla de reacción y la solución resultante fue calentada a 85 °C durante 12 horas. Se agregó agua a la mezcla de reacción para apagar la reacción. Luego se agregó EtOAc para extraer la solución acuosa. La capa de EtOAc fue secada sobre Na2SO4: El Na2SO4 fue filtrado y el filtrado fue evaporado proporcionar un residuo aceitoso de color marrón oscuro. El residuo fue purificado mediante cromatografía de gel de sílice (eluyendo con CH3OH, CH2Cl2, EtOAc, y hexanos) para proporcionar el producto deseado, compuesto A4:

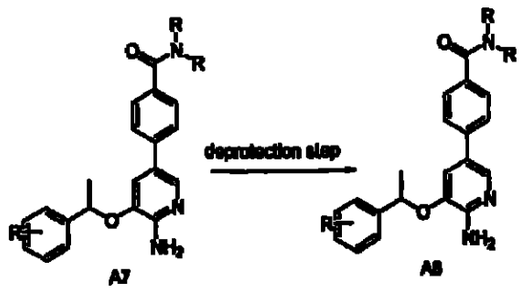
Procedimiento general 20:



El compuesto A6 fue preparado utilizando el procedimiento general 19. Pentafluoro de sodio 0- (7- azabenzotriazol- 1- il)- N,N,N′- tetrametilluronio (HATU) (1.1 molar equivalente), amina de diisopropiletilo (5 molar equivalente) y amina (1.3 molar equivalente) fueron agregados a una solución del compuesto A6 (0.17 mmol) en mL de DMF bajo una atmósfera de nitrógeno. La reacción fue dejada agitar a temperatura ambiente durante 12 horas. Se agregó NaHCO3 saturado a la mezcla de

reacción para apagar la reacción. Luego se agregó EtOAc para extraer la solución acuosa. La capa de EtOAc fue secada sobre Na2SO4. El Na2SO4 fue filtrado y el filtrado fue evaporado para proporcionar un residuo aceitoso color marrón. El residuo fue purificado mediante cromatografía de gel de sílice (eluyendo con EtOAC y hexanos) para proporcionar el producto amida deseado, compuesto A7, como un aceite amarillo.

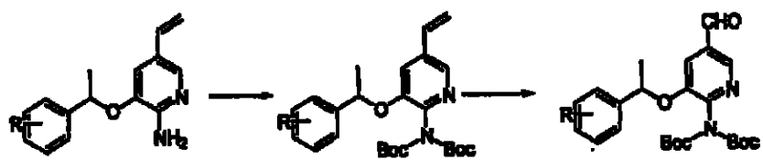
Procedimiento general 21



A7 A8

Se agregó ácido (16 molar equivalente o menos) al compuesto A7 (0.13 mmol) a temperatura ambiente. La solución resultante fue agitada a temperatura ambiente o calentada a 60 °C durante 12 horas. La mezcla de reacción fue evaporada y el residuo fue purificado mediante cromatografía de gel de sílice (eluyendo con CH3OH, EtOAc y CH2Cl2) para proporcionar el producto amida deseado, compuesto A8, como un sólido amarillento a blanco.

Procedimiento general 22

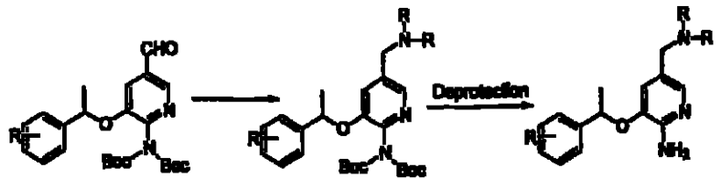


A9 A10 A11

El compuesto A9 se preparó utilizando el procedimiento general 19. Se agregó dicarbonato di- tert- butilico (3 molar equivalente) y 4- (dimetilamino)piridina (0.14 molar equivalente) a una solución del compuesto A9 (3 mmol) in 20 mL de DMF. La mezcla de reacción fue agitada a temperatura ambiente durante 12 horas. Se agregó agua a la mezcla de reacción para apagar la reacción. Luego se agregó EtOAc para extraer la solución acuosa. La de EtOAc fue secada sobre Na2SO4. El Na2SO4 fue filtrado y el filtrado fue evaporado para proporcionar un residuo aceitoso de color

amarillo marrón. El residuo fue purificado mediante cromatografía de gel de sílice (eluyendo con 25→30 % EtOAc en hexanos) para proporcionar el producto deseado, compuesto A 10 como un aceite amarillento (rendimiento 87.8%). El ozono fue burbujeado a través de una solución del compuesto A 10 en 50 mL de CH2Cl2 a- 78 °C y se agregó sulfuro de dimetil para apagar la reacción. Se agregó cloruro de sodio saturado a la mezcla de reacción y se agregó EtOAc para extraer la solución acuosa. La capa combinada de EtOAC fue secada sobre Na2So4. El Na2SO4 fue filtrada y el filtrado fue evaporado para proporcionar un residuo aceitoso amarillento. El residuo fue purificado mediante cromatografía de gel de sílice (eluyendo con 35→40 %EtOAc en hexanos) para proporcionar el producto deseado, compuesto A 11 como un aceite amarillento (rendimiento 58.4%).

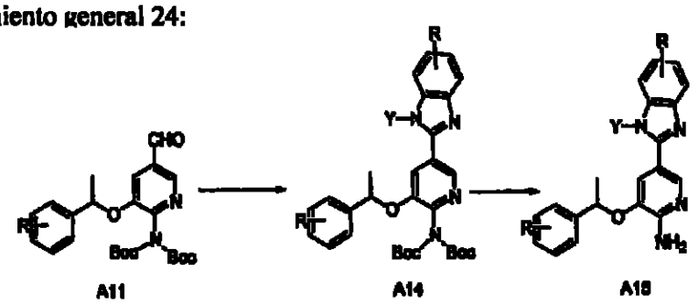
Procedimiento general 23: aminación reductiva



A11 A12 A13

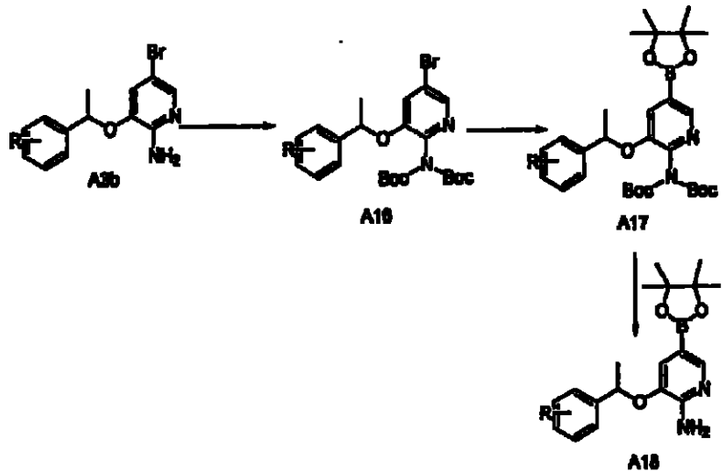
Se agregó sal de hidrocluro de amina, (1.2 equivalente molar), acetato de sodio (2 molar equivalente a la sal hidrocloruro de amina) a una solución del compuesto A11 (0.45 mmol) en 4 mL de CH3OH bajo una atmósfera de nitrógeno. Se agregó un tamiz molecuar (0.5 g) a la mezcla de reacción y luego se agregó cianobromohidruro de sodio (2 molar equivalente). La mezcla resultante fue agitada a temperatura ambiente durante 12 horas bajo atmósfera de nitrógeno. La mezcla de reacción fue filtrada a través de un lecho de Celite y el filtrado fue evaporado y purificado mediante cromatografía de gel de sílice (eluyendo CH3OH, EtOAc, y CH2Cl2) para proporcionar el producto deseado, compuesto A12 como un aceite (rendimiento 52.6%). Se agregó ácido (16 molar equivalente o menos) al compuesto A12 (0.17) a temperatura ambiente. La solución resultante fue agitada a temperatura ambiente o calentada a 60 °C durante 12 horas. La mezcla de reacción fue evaporada y el residuo fue purificado mediante cromatografía de columna (eluyendo con CH2OH, EtOAc y CH2Cl2) para proporcionar el producto deseado, compuesto A13.

Procedimiento general 24:



Se agregó O- fenildiaminas (1.2 molar equivalente) y bisulfalto de sodio a una solución del compuesto A 11 (0.41 mmol) en 5 mL de DMA. La solución resultante fue calentada a 110 °C durante 12 horas. Se agregó agua a la mezcla de reacción para apagar la reacción. Luego se agregó EtOAc para extraer la solución acuosa. La capa EtOAc fue secada sobre Na2SO4. El Na2SO4 fue filtrado y el filtrado fue evaporado para proporcionar un residuo aceitoso amarillo marrón. El residuo fue purificado mediante cromatografía de gel de sílice (eluyendo con EtOAC en hexanos)para proporcionar el producto deseado, compuesto A 14. Se agregó ácido (16 molar equivalente o menos) al compuesto A 14 (0.16 mmol) a temperatura ambiente. La solución resultante fue agitada a temperatura ambiente o calentada a 60 °C durante 12 horas. La mezcla de reacción fue evaporada y el residuo filtrado mediante cromatografía de gel de sílice (eluyendo con Ch3OH, EtOAc y CH2Cl2) para proporcionar el producto amida deseado, compuesto A 15.

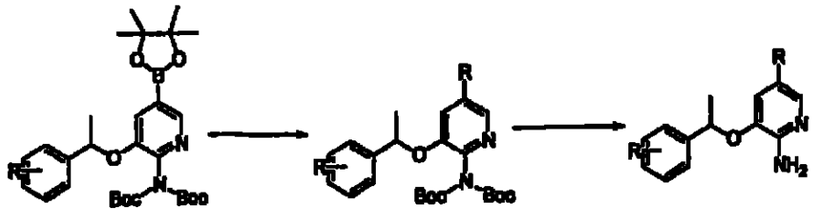
Producto general 25:



Se agregó dicarbonato di- ter- butilo (3 molar equivalente), 4-(dimetilamino)piridina (0.14 molar equivalente) a una solución del compuesto A3b (2 mmol) en 10 mL de DMF. La mezcla de reacción fue agitada a temperatura ambiente durante 12 horas. Se agregó agua a la mezcla de reacción para apagar la reacción. Luego se agregó EtOAc para extraer la solución acuosa. La capa de EtOAc fue secad sobre Na2SO4. El NaSO4 fue filtrado y evaporado para proporcionar un residuo aceitoso amarillo marrón (compuesto a 16). El residuo fue utilizado sin purificación adicional.

Se agregó bis(pinacolato)diboron (1.2 molar equivalente) y acetato de potasio (3.4 molar equivalente) a una solución del compuesto a16 en 4 mL de DMSO. La mezcla fue purgada con nitrogeno varias veces y luego se agreó diclorobis(trifenilfosfino) paladio (II) (0.05 molar equivalente). La solución resultante fue calentada a 80 °C durante 12 horas. Se agregó agua a la mezcla de reacción para apagar la reacción. Luego se agregó EtOAc para extraer la solución acusa. La capa EtOAc fue secada sobre Na2SO4. El Na2SO4 fue filtrado y el filtrado evaporado para proporcionar un residuo aceitoso marrón oscuro. El residuo fue purificado mediante cromatografía de gel de sílice (eluyendo con 30% EtOAc en hexanos) para proporcionar el producto deseado, compuesto A 17 (rendimiento 76%). Se agregó HCl (5 molar equivalente) a una solución del compuesto A17 (0.43 mmol) en 4 mL de CH2Cl2. La mezcla resultante fue calentada a 50 °C durante 12 horas. Se agregó NaHCO3 saturado a la mezcla de reacción para neutralizar la reacción. Luego se agregó EtOAc para extraer la solución acuosa. La capa EtOAc fue secada sobre Na2SO4. El Na2SO4 fue filtrado y el filtrado fue evaporado para proporcionar el producto deseado (compuesto A 18) como un solido (rendimiento 75%).

Procedimiento general 26:

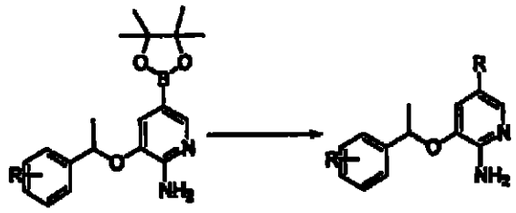


A17 A19 A20

Se agregó el compuesto A 17 (1.3 molar equivalente) a una solución de haluro de arilo (0.36 mmol) en 3 mL de DMF. La mezcla fue purgada con nitrógeno varias veces y luego se agregó diclorobis(trifenilfosfino)paladio (II) (0.05 molar equivalente).

Se agregó carbonato de sodio (3 molar equivalente) en 0.8 mL de H2O a la mezcla de reacción y la solución resultante fue calentada a 85 °C durante 12 horas. Se agregó agua a la mezcla de reacción para apagar la reacción. Luego se agregó EtOAc para extraer la solución acuosa. La capa EtOAc fue secada sobre Na2So4. El Na2SO4 fue filtrado y el filtrado evaporado para proporcionar un residuo aceitoso de color marrón oscuro. El residuo fue purificado mediante cromatografía de gel de sílice (eluyendo con EtOAC en hexanos) para proporcionar el producto deseado, compuesto A 19 (rendimiento 74.4%). Se agregó HCl (5 molar equivalente) a una solución del compuesto A 19 (0.26 mmol) en 10 mL de alcohol de isopropilo. La mezcla resultante fue calentada a 50 °C durante 12 horas. El solvente fue evaporado para proporcionar el producto deseado, compuesto A 20.

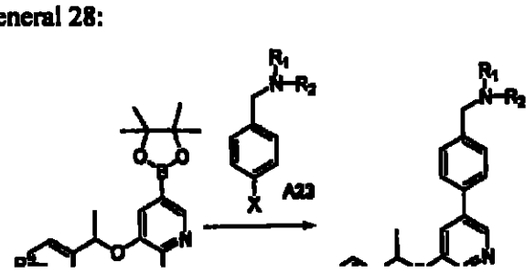
Procedimiento general 27:



A18 A21

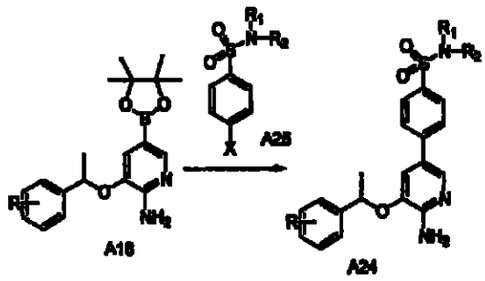
Se agregó el compuesto A 18 (1.3 molar equivalente) a una solución de haluro de arilo 80.21 mmol) en 3 mL de DMF. La mezcla de reacción fue purgada con nitrógeno varias veces y luego se agregó diclorobis(trifenilfosfino)paladio (II) (0.05 molar equivalente). Se agregó carbonato de sodio (3 molar equivalente) en 0.6 mL de H2O a la mezcla de reacción y la solución resultante fue calentada a 85 °C durante 12 horas. Se agregó agua a la mezcla de reacción para apagar la reacción. Luego se agregó EtOAc para extraer la solución acuosa. La capa EtOAc fue secada sobre Na2SO4. El Na2SO4 fue filtrado y el filtrado fue evaporado para proporcionar un residuo aceitoso de color marrón oscuro. El residuo fue purificado mediante cromatografía de gel de sílice 8eluyendo con CH3OH, CH2Cl2; EtOAc, y exanos) para proporcionar el producto deseado, compuesto A 21.

Procedimiento general 28:



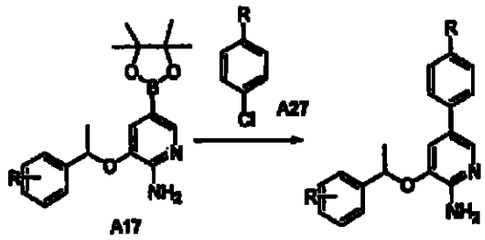
Se agregó amina (1.5 molar equivalente) y K2CO3 (1.5 molar equivalente) a una solución de haluro de halobencilo (1.0 molar equivalente) en 2 mL de tolueno. La mezcla resultante fue sometida a microondas utilizando sintetizador Smith (150 °C, 1 hora). Se agregó agua a la mezcla de reacción para apagar la reacción. Luego se agregó EtOAc para extraer la solución acuosa. La capa EtOAc fue secada sobre Na2SO4. El Na2SO4 fue filtrado y el filtrado fue evaporado para proporcionar el producto deseado, compuesto A 23. El residuo se utilizo en el procedimiento 11 sin purificación adicional para sintetizar el compuesto A 22.

Procedimiento general 29:



Se agregó amina (1.2 molar equivalente) y diisopropilamina (5 molar equivalente) a una solución de cloruro de 4- bromobencenosulfonil (0.77 mmol) en 5 mL deCHCl3 bajo una atmósfera de nitrogeno. La mezcla resultante fue agitada a temperatura ambiente durante 4 hr. Se agrego agua a la mezcla de reacción para apagar la reacción. Luego se agregó EtOAc para extraer la solución acuosa. La capa EtOAc fue secada sobre Na2SO4. El Na2SO4 fue filtrado y el filtrado fue evaporado para proporcionar el producto deseado, compuesto A 25. El residuo se utilizo en el procedimiento 11 sin purificación adicional para sintetizar el compuesto A24.

Procedimiento general 30:

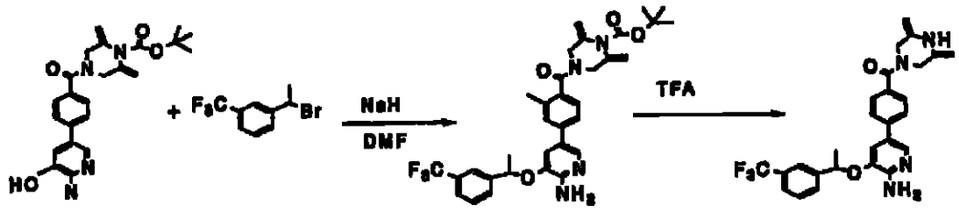


Se agregó ácido borónico o éster borónico (1.2 molar equivalente) a una solución de 1- cloro- 4- yodobenceno (0.84 mmol) en 10 mL de dimetileter del glicol de etileno (DME) bajo una atmósfera de nitrogeno. La mezcla fue purgada con nitrógeno varias veces y luego se agregó diclorobis(trifenilfosfino) paladio (II) (0.05 molar equivalente). Se agregó carbonato de sodio (3 molar equivalente) en 1.8 mL de H2O a la mezcla de reacción y la solución resultante fue calentada a 85 °C durante 12 horas. Se agregó agua a la mezcla de reacción para apagar la reacción. Luego se agregó EtOAc para extraer la solución acuosa. La capa EtOAc fue secada sobre Na2SO4. El Na2SO4 fue filtrada y el filtrado fue evaporado para proporcionar un residuo aceitoso de color marrón oscuro. El residuo fue purificado mediante gel de sílice (eluyendo con CH3OH, CH2Cl2, EtOAc, en hexanos) para proporcionar el producto deseado, compuesto A 27. El compuesto A27 fue usado en el procedimiento 11 para sintetizar el compuesto A 26.

Procedimiento General 31 para Separación Quiral de Racematos:

La muestra racemica fue purificada utilizando cromatografía preparativa de fluido supercritico SFC- MS. Las condiciones de purificación fueron: columna Chiralpak AD- H, 250 x 21 mm, 5 micras, columna 100A (Columna #: AD0CJ- C 1003); temperatura de columna 35 °C, fase movil de metanol al 35 % (con isopropilamina 0.1%)- CO2 modificado; tasa de flujo preparativo 52 mL/minuto; presión isobárica 120 barios. La quiralidad especifica de los isómeros no se determino definitivamente.

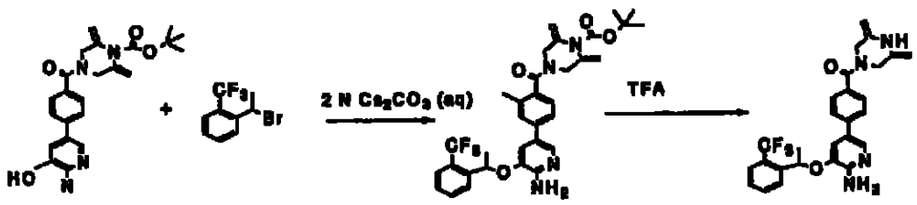
Procedimiento General 32:utilizando el Ejemplo I- 617



A una mezcla de éster tert- butilo del ácido 4- [4- (6- amino- 5- hidroxi- piridin- 3- il)- benzoil]- 2,6- dimetil- piperazina- 1- carboxilico (100mg, 0.23 mmol) y 1- (1-

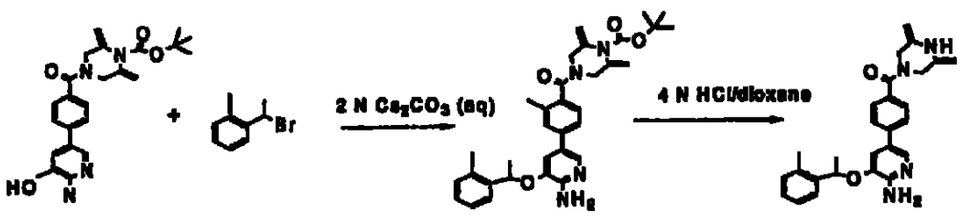
bromo- etil)- 3- trifluorometil- benzeno (64 mg, 0.25 mmol) en DMF (2 ml) se agregó NaH (12 mg, 0.47 mmol) a 0 °C. La mezcla fue agitada durante la noche. El LCMS mostró que la reacción estaba completa. Fueron removidos DMF y agua. Se agregó TFA (2 mL) al residuo y se agito a temperatura ambiente durante 3 horas. TFA fue removido seguido por adición de metanol. El residuo fue purificado mediante HPLC preparativa para proporcionar (4- {6- amino- 5- [1- (3- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- (3,5- dimetil- piperazin- 1- il)- metanona (30 mg, rendimiento 25.7 %).

Procedimiento general 33: utilizando el Ejemplo I- 616



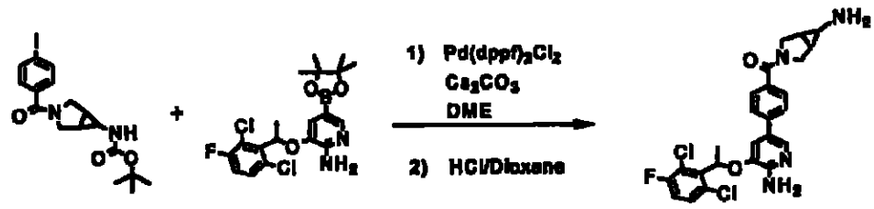
A una mezcla de éster tert- butilo del ácido 4- [4- (6- amino- 5- hidroxi- piridin- 3- il)- benzoil]- 2,6- dimetil- piperazina- 1- carboxilico (50 mg, 0.12 mmol) y 1- (1- bromo- etil)- 2- trifluorometil- benzeno (32 mg, 0.12 mmol) en DMF (2 mL) se agregó Cs2CO3 2 M (0.18 mL, o.35 mmol), seguido por agua (0.5 mL), la mezcla fue agitada durante la noche luego calentada a 70 °C durante 8 horas, LCMS mostró que la reacción fue completada. Se agregó TFA (2 mL) al residuo y se agito a temperatura ambiente durante 3 horas. El TFA fue removido, seguido por adición de metanol. El residuo fue purificado mediante HPLC preparativa para proporcionar. (4- {6- amino- 5- [1- (3- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- (3,5- dimetil- piperazin- 1- il)- metanona (20 mg, rendimiento 34.2%).

Procedimiento 34: utilizando el Ejemplo I- 624



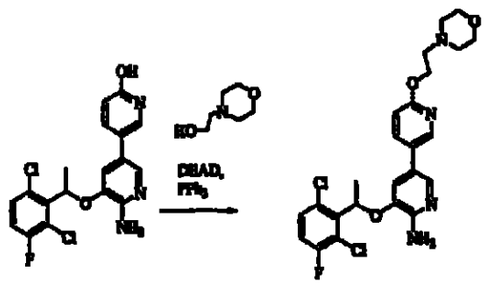
A una mezcla de éster tert- butilico del ácido (2R, 6S)- 4- [4- (6- amino- 5- hidroxi- piridin- 3- il)- benzoil]- 2,6- dimetil- piperazina- 1- carboxilico (100 mg, 0.23 mmol) y 1- bromometil- 2- metil- benceno (47 mg, 0.25 mmol) en DMF (2 mL) se agregó Cs2CO3 2M (0.35 mL, 0.7 mmol) seguido por agua (0.5 mL). La mezcla fue agitada a temperatura ambiente durante la noche. LCMS mostró que la reacción fue completada, DMF fue removido, seguido por adición de HCl 4 N en dioxano (2 mL) y la reacción fue agitada a temperatura ambiente durante 3 horas. Los compuestos volatiles fueron removidos seguido por adición en metanol. Esta solución fue purificada mediante HPLC preparativa para proporcionar (4- {6- amino- 5- (metil- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona (47 mg, rendimiento 46.6%).

Procedimiento 35: utilizando I- 635



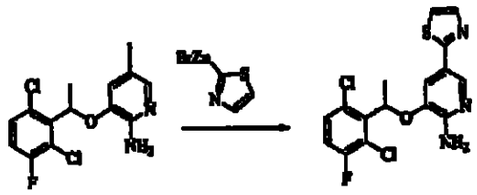
A una mezcla de éster tert- butilico del ácido[3- (4- yodo- benzoil)- 3- aza- biciclo[3.1.0]hex- 6- il]- carbamico (100 mg, 0.234 mmol) y 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- piridin- 2- ilamina (100 mg, 0. 234 mmol) en DMF (2 mL) se agregó Pd(dppf)2Cl2CH2Cl2 (10 mg, 0.012 mmol) y Cs2CO3 (351 mg, 0.702 mmol). La mezcla fue burbujeada con nitrógeno durante 10 minutos luego sometida a microondas a 150 °C durante 30 minutos. LCMS reviso que la reacción estuviera completa . La mezcla de reacción cruda fue diluida con acetato de etilo seguido por lavados con agua y salmuera. La solución fue secada sobre MgSO4. La purificación mediante HPLC preparativa proporcionó un sólido. El sólido fue agitado con HCl 4N/dioxano (3 mL) durante 3 horas a temperatura ambiente. El retiro de los compuesto volatiles llevo a un compuesto que fue purificado mediante HPLC preparativa para proporcionar (6- amino- 3- aza- biciclo[3.1.0]hex- 3- il)- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil- metanona (30 mg, rendimiento 26%)

Procedimiento 36: utilizando I- 636



A una mezcla de 6´- amino- 5´- [2,6- dicloro- 3- fluoro- fenil)- etoxi]- [3,3´]bipiridinil- 6- ol (78 mg, 0.20 mmol), trifenifosfina (63 mg, 0.24 mmol) y 2- morfolin- 4- il- etanol (0.026 mL,0.22 mmol) se agregó DEAD (0.034 mL, 0.22 mmol). Después de agitar durante la noche más PPh3 (63 mg, 0.24 mmol) y mas DEAD (0.034 mL, 0.22 mmol). Después de varias horas, se agregó mas alcohol (0.026 mL, 0.22 mmol). Después de varias horas se agregó mas PPh3 (63 mg, 0.24 mmol) y mas DEAD (0.034 mL, 0.22 mmol). Después de agitar durante la noche, la mezcla fue particionada entre diclorornatano y salmuera medio saturada. Las fases fueron saturadas y la fase acuosa fue extraída con diclorometano. Las fases orgánicas combinadas fueron secadas sobre Na2SO4 y concentradas mediante evaporación rotatoria. El residuo fue purificado mediante cromatografía de gel de sílice utilizando elusión de gradiente de diclorometano, metanol para proporcionar 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 6´- (2- morfolin- 4- il- etoxi)- [3,3`]bipiridinil- 6- ilamina (53 mg, 53%).

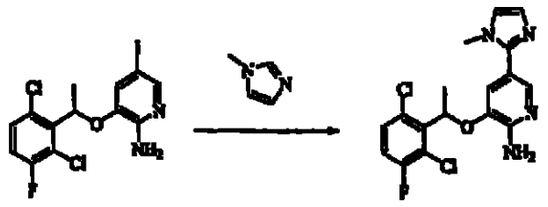
Procedimiento 37: utilizando el Ejemplo I- 650



3- (2,6- diclorometano- 3- fluoro- benciloxi)- 5- tiazol- 2- il- piridin- 2- ilamina: a un tubo de microondas equipado con una barra de agitación se agregó el material de inicio yodo- oiridilo (300 mg, 0.702 mmol), tetrakis- (trifenilfosfina) paladio (0) (40 mg, 5 mol%) y tetrahidrofuran (anhidro, 6 mL). El frasco fue tapado y purgado con nitrógeno durante 5 minutos. Luego se agregó bromuro de 2- tiazolizinc (0.5 M en THF, 1.4 mmol, 2.8 mL) mediante jeringa. El frasco fue calentado 120 °C en el microondas durante 10 minutos. TLC (1:1 acetato de etilo: cloruro de metileno) mostró un gran

cantidad de material de inicio remanente. Se agregó bromuro de 2- tiazolylzinc (0.5 M en THF, 500 µL) adicional y el frasco fue calentado a 120 °C en el microondas durante 20 minutos. TLC (1:1 acetato de etilo: cloruro de metileno) mostró un gran cantidad del material de inicio aún remanente. Se agregó bromuro de 2- tiazolilzinc 80.5 M en THF, 500 µL) y el frasco fue calentado a 120 °C en el microndas durante 60 minutos. TLC (1.1 acetato de etilo: cloruro de metileno) aún mostró una gran cantidad de material de inicio aún remanente pero también se había vuelto bastante desordenado. Los contenidos del frasco fueron vertidos entre una solución NH4Cl saturado (10 mL) y esta solución extraída con acetato de etilo (2 x30 mL). Las capas de acetato de etilo fueron secadas sobre Na2SO4, filtradas y concentradas al vacío. El producto crudo fue cargado sobre una columna de gel de sílice pre- empacado y 1:1 acetato de etilo: cloruro de metileno usado para extraer el producto deseado. (40 mg, 15%).

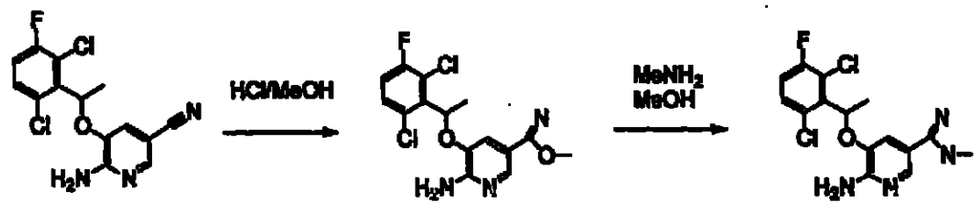
Procedimiento 38 utilizando el Ejemplo I- 652



3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (1- metil- 1H- imidazol- 2- il)- piridin- 2- ilamina: imidazol de N- metilo (92 mg, 1.1 mmol) fue disuelto en tetrahidrofurano (anhidro, 4 mL) en una matraz de fondo redondo 50 mL. La matraz fue enfriada con un baño seco- hielo/acetona bajo atmósfera de nitrógeno. Se agregó litio de N- butilo (2.5 M, 562 µL, 1.4 mmol) mediante jeringa en porciones 100 µL durante 5 minutos. La reacción fue agitada a –70°C durante 30 minutos. Se agregó cloruro de zinc solido (anhidro, 383 mg, 2.8 mmol) y la reacción se agito durante 15 minutos. El baño de hielo fue luego removido y la reacción se dejo calentar a temperatura ambiente. Una vez agregado todo el cloruro de zinc en solución y la reacción a temperatura ambiente, se agregó armazón de yodo (400 mg, 0.936 mmol) en tetrahidrofurano (anhidro, 4 mL), seguido por tetrakis(trifenilfosfina)paladio (0) (108 mg, 10 mmol%) y la reacción calentada hasta reflujo. La reacción fue monitoreada mediante LC/MS hasta consumir todo el armazón de yodo de inicio. La reacción fue dejada enfriar y luego diluida con una solución NH4Cl saturada (20 mL). Esta solución fue extraída con acetato de etilo (2

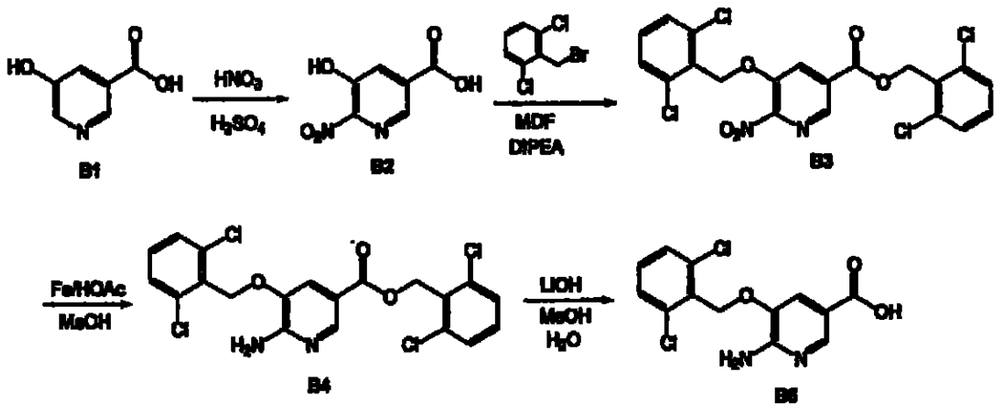
x 50 mL). Las capas combinadas de acetato de etilo fueron secadas sobre Na2SO4, filtradas y concentradas al vacío. El producto crudo fue cargado sobre una columna de gel sílice pre- empacada 10 g y se utilizo metanol 10%: acetato de etilo para usado eluir el producto deseado (25 mg, 7%)

procedimiento general 39: utilizando el Ejemplo I- 657



A 6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- nicotinonitrilo (400 mg, 1.23 mmol) en 70 mL de metanol seco a 0°C se burbujeó gas HCl durante 3 minutos. Se agitó durante la noche a 3°C. Los compuestos volatiles fueron removidos y lavados con éter dietílico para proporcionar cuantitativamente el imidato. A 200 mg del imidato en 4 mL metanol a 0°C se agregó metilamina 2N en THF (837 µL). Se dejo agitar a 0°C durante 1 hora aproximadamente y luego se dejo calentar a temperatura ambiente durante la noche. Los compuestos volatiles fueron removidos y el residuo fue cromatograficado con metanol al 10- 20% /diclorometano para proporcionar 70 mg del producto.

Procedimiento general 40:



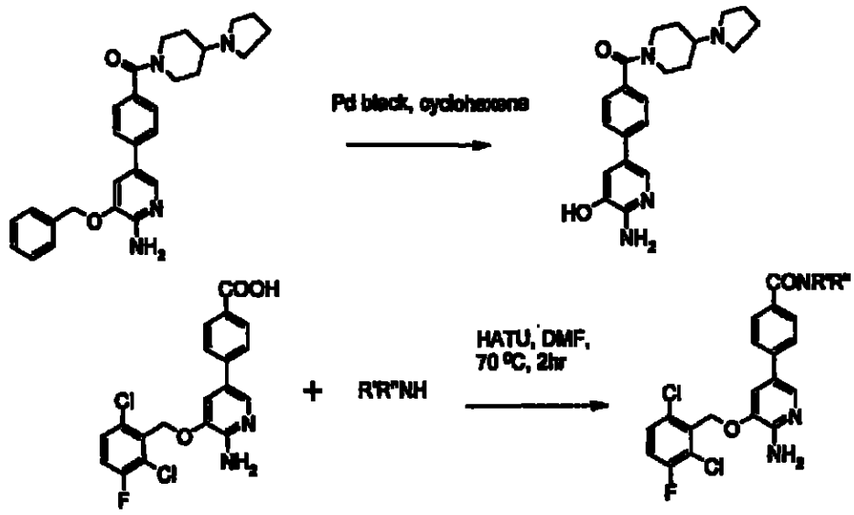
1. Acido 6- Nitro- 5- hidroxinicotinico (B2): a una solución de ácido 5- hidroxinicotinico (B1) (7.0 g, 50 mmol) en H_2SO_4 concentrado se agregó a 9 mL de HNO_3 fumante (90%) (9 mL). La mezcla de reacción fue agitada a 55- 60°C en un tubo sellado durante 4 días. Luego la mezcla fue vertida en hielo y el pH fue ajustado a 3 con NaOH al 50%. Se agregó $MgSO_4$ para saturar la mezcla acuosa, la cual luego se extrajo con alcohol isopropílico (4x4 mL). Después de remover el alcohol isopropílico bajo presión reducida, 5.93 g (rendimiento 64%) de B2 fue obtenido como un sólido amarillo. MS (APCl).$(M+H)^+$ 185. ^{1}HNMR (DMSO- d6) δ 8.01 (d, 1H, Ar- H), 8.41 (d, 1H, Ar- H).

2. 2,6- diclorobencil- 6- nitro- 5- [(2,6- diclorobencil)oxi]nicotinato (B3): ácido 6- nitro- 5- hidroxinicotinico (B2) (3.4 g, 18.5 mmol), bromuro de 2,6- diclorobencil (8.88 g, 37 mmol), DIPEA (5.5 g, 42.5 mmol) fueron disueltos en DMF (25 mL) en una matraz de fondo redondo de 250 mL y la reacción fue agitada a temperatura ambiente durante 4.5 horas y luego concentrada bajo presión reducida. La mezcla resultante fue vertida en hielo y filtrada. El sólido recolectado fue secado bajo presión reducida para proporcionar 4.25 g (rendimiento 46%) de B3. MS (APCl) $(M+H)^+$503. ^{1}HNMR (DMSO- d6) δ 5.47 (s, 2H, $ArCH_2O$), 5.71 (s, 2H, $ArCH_2O$), 7.24- 7.43 (m, 6H, Ar- H), 8.26 (d, 1H, Ar- H), 8.66 (d, 1H, Ar- H).

3. 2,6- diclorobencil- 6- amino- 5- [(2,6- diclorobencil)oxi]nicotidina (B4): una mezcla de 2,6- diclorobencil- 6- nitro- 5- [(2,6- diclorobencil)oxi] (B3) (5.5. g, 10.96 mmol), polvo de hierro (0.92 g, 16.43 mmol), ácido acético glacial (20 mL) y metanol (17 mL) fue agitada 85°C durante tres horas. La mezcla de reacción fue concentrada hasta casi sequedad, y se agregó hidróxido de amonio (30%) para neutralizar la mezcla. Se agregó una cantidad mínima de DMF para disolver la mezcla de reacción. La cual se purificó mediante cromatografía de columna rápida (eluyendo: EtOAc- EtOH, 9:1) para proporcionar 4.5 g (87%) de B4 como un sólido de color amarillo pálido. Ms (APCl) $(M+H)^+$ 473.

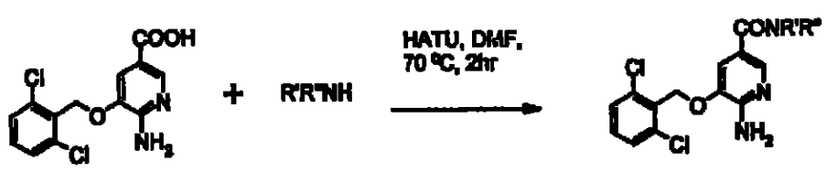
4. Acido 6- amino- 5- [(2,6- diclorobencil)oxi]nicotínico (B5): una mezcla de 2,6- diclrobencil- 6- amino- 5- [(2,6- diclorobencil)oxi]nicotinato (B4) (3.5 g, 7.4 mmol), hidroxido de litio (0.41 g, 17 mmol), agua (22 mL) y metanol (30 mL) fue agitada y sometida a reflujo a 85°C durante 5 horas. La mezcla fue concentrada hasta sequedad bajo presión reducida. El residuo resultante fue disuelto en agua, extraído con una mezcla de Et_2O/hexano (1:1 4x25 mL), neutralizado con HCl 1N para formar

precipitado blanco, el cual fue filtrado y secado bajo presión reducida para proporcionar 1.83 gramos (79%) de B5 como un sólido de color blanco. MS (APCI) $(M+H)^+$ 313. ^{1}HNMR (DMSO- d6) δ 5.26 (s, 2H, ArCH2O), 6.37 (s, 2H, NH2), 7.43- 7.48 (t, 1H, Ar- H), 7.54 (s, 2H, Ar- H),7.56 (s, 1H, Ar- H), 8.18 (s, 1H, Ar- H).



A un arreglo de 400 µL de solución 0.2 M de diferentes aminas en DMF en una placa de 96 pozos se agregó 400µL (0.2 M en DMF) de ácido 4- [6- amino- 5- (2,6- dicloro- 3- fluoro- benciloxi)- piridin- 3- il]- benzóico, 80 µL de trietilamina (1 M en DMF) y 160 µL de HATU (0.5 M en DMF) y las reacciones fueron agitadas a 70°C durante 12 horas. El solvente fue removido utilizando el aparato SpeedVac y las mezclas de reacción crudas fueron disueltas nuevamente en DMSO y transferidas utilizando un manejador de líquidos a una placa de 96 pozos para proporcionar una concentración teórica final de ~10 mM. Las reacciones fueron analizadas y se hizo identificación positiva del producto utilizando LC/MS. La solución madre fue diluida a 50 nM y sometida a ensayo para porcentaje de inhibición de c- MET a 50 nM

Procedimiento general 41



A un arreglo de 400 µL de solución de diferentes aminas en DMF una placa de 96 pozos se agregó 400 µL (0.2 M en DMF) de ácido 6- amino- 5- [(2,6- diclorobencil)oxi]- nicotinico, 80 µL de trietilamina (1M en DMF) y 160 µL de HATU (0.5 M en DMF) y las reacciones fueron agitadas a 70°C durante 2 horas. El solvente fue removido utilizando el aparato SpeedVac y las mezclas de reacción crudas fueron disueltas nuevamente en DMSO y transferidas utilizando un manejador de líquido a una placa de 96 pozos para proporcionar una concentración teórica final de ~10 mM. Las reacciones fueron analizadas y se hizo identificación positiva del producto utilizando LC/MS. La solución madre fue diluida a 1 µM y sometida a ensayo.

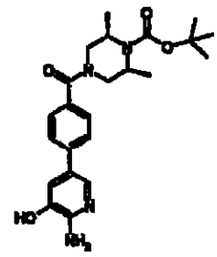
Procedimiento general 42

[4- (6- amino- 5- hidroxi- piridin –3- il)- fenil]- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona: una solución de [4- (6- amino- 5- benciloxi- piridin –3- il)- fenil]- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona (3.67 g, 8.1 mmol) en 100 ml de etanol se agregó 25 mL de ciclohexeno y 367 mg negro de paladio. Se sometió a reflujo durante la noche. La solución fue filtrada y los compuestos volátiles fueron removidos. Al residuo se agregó 60 mL de MeOH, 20 mL de ciclohexeno y 350 mg de negro de paladio. Se sometió a reflujo durante la noche. Se filtró y los compuestos volátiles se retiraron, se suspendió nuevamente en metanol, se agregó 350 mg de negro de paladio y se hidrogeno a 1 atm durante la noche (reactores de presión todos ocupados). Se filtró y aisló 3.0 gramos de espuma sólida. ^{1}HNMR (400 MHz, DMSO- D6) δ ppm 7.82 (d, J= 2.02 Hz, 1H), 7.58 (d, J=8.34 Hz, 2H), 7.41 (d, J=8.34 Hz, 2H), 7.12 (d, J=2.02 Hz, 1H), 5.74 (s, 2H), 3.33 (s, 5H), 3.08 (s, 2H), 1.95 (m, 8H), 1.49 (s, 2H). LC/MS(APCl) 367 m/e (M+1).

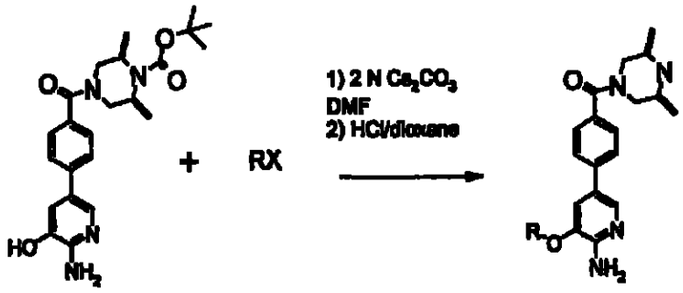
A un arreglo de tubos de prueba de 10 x 75 mm se agregó [4- (6- amino- 5- hidroxi- piridin- 3- il)- fenil]- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona (0.2 M en DMF,80 µmol, 1.0 eq), Cs2CO3 (2 M, 160 µmol, 2.0 equivalente) y diferentes haluros de alkilo (0.2 M en DMF, 88 µmol, 1.1 eq). Las reacciones fueron agitadas a temperatura ambiente durante la noche. Con el objeto de separar las sales inorgánicas, la suspención resultante fue evaporada y se agregó DMF (625 µL). Después de agitación,

la mezcla fue centrifugada para asentar el residuo sólido, y el sobre nadante fue transferido a un nuevo tubo de prueba. Las reacciones fueron analizadas y se hizo identificación positiva del producto utilizado LC/MS. La solución madre fue diluida a 1 µM y sometida a ensayo.

Procedimiento general 43:



Éster tert- butilico del ácido (2R, 6S)- 4- [4- (6- amino- 5- hidroxi- piridin- 3- il)- benzoil]- 2,6- dimetil- piperazina- 1- carboxilico. Ver procedimiento general IG. Rendimiento 83.5%. ^{1}HNMR (400 MHz, DMSO- D6) δ ppm 7.81 (d, J= 2.27 Hz, 1H), 7.57 (d, J=8.34 Hz, 2H), 7.41 (d, J=8.34 Hz, 2H), 7.12 (d, J=2.02 Hz, 1H), 5.70 (s, 2H), 4. 07 (s, 2H), 3.31 (s, 3H), 1.39 (s, 10H), 1.03 – 1.14 (m, 7H).



A un arreglo de tubos de prueba de 10 x 75 mm se agregó [4- (6- amino- 5- hidroxi- piridin- 3- il)- fenil]- (4- pirrolidin- 1- piperidin- 1- il)- metanona (0.2 M en DMF, 80 µmol, 1.0 eq), Cs2CO3 (2 M, 160 µmol, 2.0) y diferentes haluros de alkilo (0.2 M en DMF, 88 µmol 1.1 eq). Las reacciones fueron agitadas atemperatura ambiente durante la noche. Con el objeto separar las sales orgánicas, la suspención resultante fue evaporada y se agregó DMF (625 µL). Después de agitar, la mezcla fue centrifugada para asentar el residuo sólido, y el sobre nadante fue transferido a un nuevo tubo de

prueba. Los residuos sólidos fueron extraídos con mas DMF (400 µL) y los extractos fueron combinados con la primera capa orgánica. El DMF fue evaporado, y se agregó HCl (4 M en dioxano; 2.5 mmol, 31 eq) a la mezcla de reacción recibida en el tubo de prueba. La mezcla de reacción fue agitada a temperatura ambiente durante 3 horas. Las reacciones fueron analizadas y se hizo identificación positiva del producto utilizado LC/MS. La solución madre fue diluida a 1 µM y sometida a ensayo.

Ejemplo I (a):

1. A una solución agitada de Cs2CO3 (11.63 g; 35.69 mmol) en DMF (180 mL) bajo una atmósfera de N2 conteniendo 3- hidroxi- 4- nitro- piridina (5 g, 35.69 mmol) se agregó bromuro de 2,6- diclorobencil (8.56 g, 35.69 mmol). La mezcla fue agitada durante 6 horas a temperatura ambiente. La reacción fue luego diluida con H2O (100 mL). La capa acuosa fue extraída con EtOAc (2 x 50 mL). Las capas orgánicas fueron luego combinadas y lavadas con H2O (2 x 50 mL) y salmuera (1 X50 mL). Las orgánicas fueron secados sobre Na2SO4 filtradas y concentradas hasta sequedad al vacío para proporcionar 3- (2,6- dicloro- benciloxi)- 2- nitro- piridina (10.5 g, 98.4 %) como un sólido de color blanco.

2. A una mezcla agitada de AcOH (650 mL) y EtOH (500 mL) se suspendio 3- (2,6- dicloro- benciloxi)- 2- nitro- piridina (37.4 g, 0.11 mol) y trozos de hierro (69.4 g,0.11 mol). La reacción fue calentada lentamente hasta reflujo y dejada agitar durante 1 hora. La reacción fue enfriada a temperatura ambiente luego filtrada a través de un cojín de Celite. El filtrado resultante fue neutralizado con NH4OH concentrado (600 mL) y luego extraída con EtOAc (3 x 500 mL). Los extractos orgánicos combinados fueron lavados NaHCO3 saturado (2 x 100 mL), H2O (2 x 100 mL) y salmuera (1 x 100 mL) luego secadas sobre (NaSO4) filtrados y evaporados hasta sequedad al vacío para proporcionar 3- (2,6- dicloro- benciloxi)- piriidn- 2- ilamina (32.4 g, 0.11 mol, 99%) como un sólido amarillo claro. ^{1}HNMR (400 MHz, DMSO- D6) δ 7.56 (m, 3H), 7.46 (dd, 2H), 7.36 (d, 1H), 6.62 (dd, 1H), 6.18 (br s, 2H,NH2), 5.24 (s, 2H); MS m/z 270 [M+1].

3. Una solución agitada de 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina (32.4 g, 0.11 mol) en acetonitrilo fue enfriada a 0°C utilizando un baño de hielo. A esta solución se agregó N- bromosuccinimida (19.5 g, 0.11 mol) por porciones. La reacción fue agitada a 0°C durante 15 minutos. La reacción fue concentrada hasta sequedad al vacío. El aceite oscuro resultante fue disuelto en EtOAc (500 mL) y particionado con

H2O (250 mL). La capa orgánica fue luego lavada con NaHCO3 saturado (2 x 200 mL) y salmuera (1 x 200 mL). Se agregó carbón de leña activado a la capa orgánica y calentada hasta reflujo. Luego la solución fue enfriada a temperatura ambiente y filtrada a través de un cojín de Celite. Luego la capa orgánica fue concentrada hasta sequedad al vacío hasta un tercio del volumen original. Luego los sólidos fueron filtrados para proporcionar 5- bromo- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina (22.0 g, 0.07 mol, 64%) como un sólido de color canela. El filtrado restante fue concentrado al vacío para proporcionar 5- bromo- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina (12.1 g, 0.04 mol, 35%) como un solido de color marrón.

Ejemplo I(b): 3- benciloxi- 5- bromo- piridin- 2- ilamina fue preparada siguiendo el procedimiento 1 a partir de 3- benciloxi- 5- piridin- 2- ilamina como un sólido color canela en rendimiento de 65%.

Ejemplo I(c): 5- bromo- 3- (2,6- difluoro- benciloxi)- piridin- 2- ilamina se preparó siguiendo el procedimiento 1 3- (2,6- difluoro- benciloxi)- 2- nitro- piridina fue preparada en rendimiento de 99% ^{1}HNMR (400 MHz, DMSO- d6) δ 8.14 (m, 2H), 7.79 (dd, 1H), 7.52 (m, 1H), 7.16 (m, 2H), 5.37 (s, 2H); Ms m/z 266 [M+]. 3- (2,6- difluoro- benciloxi)- piridin- 2- ilamina fue preparado en rendimiento de 100% ^{1}HNMR (400 MHz, DMSO- d6) δ 7.88 (s, 2H), 7.64 (dd, 1H), 7.57 (m, 2H), 6.84 (dd, 1H), 5.24 (s, 2H); Ms m/z 237[M+1]; 5- bromo- 3- (2,6- difluoro- benciloxi)- piridin- 2- ilamina fue preparado en rendimiento del 91%.

Ejemplo I(d): 5- bromo- 3- (2- bromo- benciloxi)- piridin- 2- ilamina se preparo siguiendo el procedimiento 1. El intermedio 3- (2- bromo- benciloxi)- 2- nitro- piridina se preparó en rendimiento del 99 % como un sólido de color blanco 3- (2- bromo- benciloxi)- piridin- 2- ilamina fue preparada en rendimiento del 100% como un sólido. 5- bromo- 3- (2- bromo- benciloxi)- piridin- 2- ilamina fue obtenida en rendimiento del 37% como un sólido color canela.

Ejemplo I(e): 5- bromo- 3- (2- cloro- 6- fluoro- benciloxi)- piridin- 2- ilamina fue preparada siguiendo el procedimiento 1. 3- (2- cloro- 6- fluoro- benciloxi)- 2- nitro- piridina fue preparada en rendimiento del 90% como un sólido de color blancuzco ^{1}HNMR (400 MHz, DMSO- d6) δ 8.15 (m, 2H), 7.80 (m, 1H), 7.50 (m, 1H), 7.40 (m, 1H), 7.30 (m, 1H), 5.39 (s, 2H). 3- (2- cloro- 6- fluoro- benciloxi)- piridin- 2- ilamina fue preparada en rendimiento del 88% como un sólido de color canela. ^{1}HNMR (400

MHz, DMSO- d6) δ 7.70- 7.15 (m, 5H), 6.45 (m, 1H), 5.45 (br s, 2H), 5.06 (s, 2H). 5- bromo- 3- (2- cloro- 6- fluoro- benciloxi)- piridin- 2- ilamina fue preparado en rendimiento del 81%.

Ejemplo I(f): 5- bromo- 3- (2- cloro- 4- fluoro- benciloxi)- piridin- 2- ilamina fue preparada siguiendo el procedimiento 1. 3- (2- cloro- 4- fluoro- benciloxi)- 2- nitro- piridina fue preparada en rendimiento del 91% como un sólido de color blancuzco ^{1}HNMR (400 MHz, DMSO- d6) δ 8.08 (m, 2H), 7.75 (m, 1H), 7.63 (m, 1H), 7.55 (m, 1H), 7.25 (m, 1H), 5.45 (s, 2H). 3- (2- cloro- 4- fluoro- benciloxi)- piridin- 2- ilamina fue preparada en rendimiento del 100% como un sólido. ^{1}HNMR (400 MHz, DMSO- d6) δ 7.70 (m, 2H), 7.47 (m, 1H), 7.20 (m, 1H), 7.08 (m, 1H), 6.45 (m, 1H), 5.62 (br s, 2H), 5.08 (s, 2H). 5- bromo- 3- (2- cloro- 4- fluoro- benciloxi)- piridin- 2- ilamina fue preparada en rendimiento del 63%.

Ejemplo I(g): 5- bromo- 3- (2,4- dicloro- benciloxi)- piridin- 2- ilamina fue preparada siguiendo el procedimiento 1. 3- (2,4- dicloro- benciloxi)- 2- nitro- piridina fue preparada en rendimiento del 91% como un sólido de color blancuzco ^{1}HNMR (400 MHz, DMSO- d6) δ 8.05- 7.50 (m, 6H), 5.39 (s, 2H); MS (m/z) 299 (M+1). 3- (2,4dicloro- benciloxi)- piridin- 2- ilamina fue preparada en rendimiento del 98% como un sólido. ^{1}HNMR (400 MHz, DMSO- d6) δ 7.65- 6.25 (m, 6H), 5.85 (br s, 2H), 5.06 (s, 2H). 5- bromo- 3- (2,4- dicloro- benciloxi)- piridin- 2- ilamina fue preparada en rendimiento del 63%.

Ejemplo I(h): 2- (2- amino- 5- bromo- piridin- 3- iloximetil)- benzonitrilo fue preparado siguiendo el procedimiento 1. 2- (2- nitro- piridin- 3- iloximetil)- benzonitrilo fue preparado en rendimiento del 91% como un sólido de color blancuzco ^{1}HNMR (400 MHz, DMSO- d6) δ 8.15- 7.55 (m, 1H), 5.50 (s, 2H). 2- (2- amino- piridin- 3- iloximetil)- benzonitrilo fue preparado en rendimiento del 86% como un sólido de color canela. ^{1}HNMR (400 MHz, DMSO- d6) δ 7.95- 6.45 (m, 7H), 5.85 (br s, 2H), 5.20 (s, 2H). 2- (2- amino- 5- bromo- piridin- iloximetil)- benzonitrilo fue preparado en rendimiento del 77%.

Ejemplo I(i): 5- bromo- 3- (2- trifluorometil- benciloxi)- piridin- 2- ilamina fue preparada siguiendo el procedimiento 1. 3- (2- trifluorometil- benciloxi)- 2- nitro- piridina fue preparada en rendimiento del 92% como un sólido de color blancuzco. ^{1}HNMR (400 MHz, DMSO- d6) δ 8.05- 7.58 (m, 7H), 5.45 (s, 2H); 3- (2- trifluorometil- benciloxi)- piridin- 2- ilamina fue preparada en rendimiento del 80% como un sólido de color canela. 5- bromo- 3- (2- cloro- 4- fluoro- benciloxi)- piridin- 2- ilamina fue preparada en rendimiento del 43% como un sólido.

Ejemplo I(j): 5- bromo- 3- (4- ter- butilo- benciloxi)- piridin- 2- ilamina fue preparada siguiendo el procedimiento 1. 3- (4- tert- butilo- benciloxi)- 2- nitro- piridina fue preparada en rendimiento del 80% como un aceite ^{1}HNMR (400 MHz, DMSO- d6) δ 8.10- 7.30 (m, 7H), 5.30 (s, 2H), 1.25 (s, 9H). 3- (4- tert- butilo- benciloxi)- piridin- 2- ilamina fue preparada en rendimiento del 100% como un sólido de color canela. ^{1}HNMR (400 MHz, DMSO- d6) δ 7.45- 6.25 (m, 7H), 5.58 (br s, 2H), 5.05 (s, 2H). 5- bromo- 3- (4- tert- butilo- benciloxi)- piridin- 2- ilamina fue preparada en rendimiento del 55% como un sólido.

Ejemplo I(k): 5- bromo- 3- (2- cloro- benciloxi)- piridin- 2- ilamina fue preparada siguiendo el procedimiento 1. 3- (2- cloro- benciloxi)- 2- nitro- piridina fue preparada en rendimiento del 89% como un sólido de color blancuzco ^{1}HNMR (400 MHz, DMSO- d6) δ 8.10- 7.40 (m, 7H), 5.40 (s, 2H). 3- (2- cloro- benciloxi)- piridin- 2- ilamina fue preparada en rendimiento del 100% como un sólido de color canela. ^{1}HNMR (400 MHz, DMSO- d6) δ 8.65- 6.45 (m, 7H), 5.62 (br s, 2H), 5.10 (s, 2H). 5- bromo- 3- (2- cloro- benciloxi)- piridin- 2- ilamina fue preparada en rendimiento del 22% como un sólido:

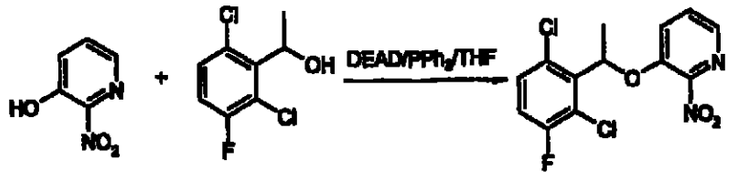
Ejemplo I(l): 5- bromo- 3- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 2- ilamina fue preparada siguiendo el procedimiento 1. El intermedio 3- (2- cloro- 3,6- difluoro- benciloxi)- 2- nitro- piridina se preparó en rendimiento del 99% como un sólido de color blancuzco. ^{1}HNMR (CDCl3, 300 MHz) δ 5.31 (s, 2H), 7.02- 7.09 (dt, 1H, J, 4, 8), 7.17- 7.23 (dt, 1H, J, 4,5,8,4), 7.54- 7.58 (dd, 1H, J, 4.5.8.4), 7.71- 7.68 (dd, 1H, J, 1.21, 8.4), 8.14- 8.16 (dd, 1H, J, 1.23, 4.5). 3- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 2- ilamina fue preparada en rendimiento del 100% como un sólido de color amarillo claro.

^{1}HNMR (CDCl3 300 MHz) δ 4.6- 4.8 (brs, 2H), 5.2 (s, 2H), 7.0- 7.08 (dt, 1H, J, 4.1, 9.0) 7.09- 7.12 (dd, 1H, J, 1.0, 7.8), 7.15- 7.22(dt, 1H, J, 1.2,5.1). 5- bromo- 3- (2-· cloro- 3,6- difluoro- benciloxi)- piridin- 2- ilamina fue obtenido en rendimiento del 64% como un sólido de color canela.

Ejemplo I(m): 5- bromo- 3- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 2- ilamina fue preparada siguiendo el procedimiento 1 de inicio a partir de 3- hidroxi- 4- nitro- piridina y brometil- 3- fluoro- 2- trifluorometil- benzeno.

Ejemplo I(n):

1. Se agitó 2,6- dicloro- 3- fluorocaetofenona (15 g, 0.072 mol) en THF (150 mL, 0.5M) a 0°C utilizando un baño de hielo durante 10 minutos. Se agregó hidruro de litio aluminio (2.75 g, 0.072 mol) lentamente. La reacción fue agitada a temperatura ambiente durante 3 horas. La reacción fue enfriada con un baño de hielo, y se agregó agua (3 mL) por goteo seguido por adición NaOH al 15% (3 mL) lentamente. La mezcla fue agitada a temperatura ambiente durante 30 minutos. Se agregó NaOH al 15% (9 mL), MgSO4 y la mezcla filtrada para remover los sólidos. Los sólidos fueron lavados con THF y el filtrado fue concentrado para proporcionar 1- (2,6- dicloro- 3- fluoro- fenil)- etanol (14.8 gm, rendimiento 95%) como un aceite amarillo. ^{1}H NMR (400 MHz, DMSO- d6) δ 1.45 (d, 3H), 5.42 (m, 2H), 7.32 (m, 1H),7.42 (m, 1H).



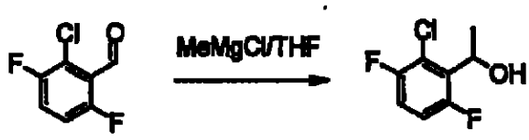
2. A una solución agitada de fosfina de trifenilo (8.2 g, 0.03 mol) y DEAD (13.65 mL de una solución en tolueno al 40%) en THF (200 mL) a 0°C se agregó una solución de 1- (2,6- dicloro- 3- fluoro- fenil)- etanol (4.55 g, 0.021 mol) y 3- hidroxi- nitropiridina (3.35 g, 0.023 mol) en THF (200 mL). La solución de color naranja claro resultante fue agitada bajo atmósfera de nitrógeno a temperatura ambiente durante 4 horas en cuyo punto todos los materiales de inicio fueron consumidos. El solvente fue removido, y el material crudo fue cargado en gel de sílice seco y eluido con acetato de hexanos de etilo (20:80) para proporcionar 3- (2,6- dicloro- 3- fluro- benciloxi9- 2- nitro- piridina (6.21 g, 0.021 mol, 98%) como un sólido rosado. ^{1}H NMR (CDCl3 300

MHz) δ 8.1- 1.85 (d, 3H), 6.0- 6.15 (q , 1H), 7.0- 7.1 (t, 1H), 7.2- 7.21 (d, 1H), 7.25- 7.5 (m, 2H), 8.0- 8.05 (d, 1H).

3. 3- (2,6- dicloro- 3- fluoro- benciloxi)- piridin- 2- ilamina fue preparada siguiendo el procedimiento 1. A una mezcla de AcOH (650 mL) y EtOH (500 mL) se suspendio 3- (2,6- dicloro- 3- fluoro- benciloxi)- 2- nitro- piridina (9.43 g, 0.028 mol) y trozos de hierro (15.7 g, 0.28 mol). La reacción fue calentada lentamente hasta reflujo y se dejo agitar durante 1 hora. La reacción fue enfriada a temperatura ambiente luego se agregó éter dietílico (500 mL) y agua (500 mL). La solución fue cuidadosamente neutralizada por la adición de carbonato de sodio. Los extractos orgánicos fueron lavados con NaHCO3 saturado (2 x 100 mL), H2O (2 x 100 mL) y salmuera (1 x 100 mL) luego secados sobre (NaSO4), filtrados y concentrados hasta sequedad al vacío para proporcionar 3- (2,6- dicloro- 3- fluro- benciloxi)- piridin- 2- ilamina (9.04 g, 0.027 mol, 99%) un sólido rosado claro. ^{1}H NMR (CDCl3 300 MHz) δ 1.8- 1.85 (d, 3H), 4.9- 5.2 (brs , 2H), 6.7- 6.84 (q, 1H), 7.0- 7.1 (m, 1H), 7.2- 7.3 (m, 1H), 7.6- 7.7 (m, 1H).

4. 5- bromo- 3- (2,6- dicloro- 3- fluro- benciloxi)- piridin- 2- ilamina fue preparado siguiendo el procedimiento 1. Una solución agitada de 3- (2,6- dicloro- 3- fluoro- benciloxi)- piridin- 2- ilamina 89.07 g, 0.03 mol) en acetonitrilo fue enfriada a 0°C utilizando un baño de hielo. A esta solución se agregó NBS (5.33 g, 0.03 mol) en porciones. La reacción fue agitada a 0°C durante15 minutos. La reacción fue concentrada hasta sequedad al vacío. El aceite oscuro resultante fue disuelto en EtOAc (500 mL) y purificado a través de cromatografía de gel de sílice. Los solventes fueron luego removidos al vacío para proporcionar 5- bromo- 3- (2,6- dicloro- 3- fluoro- benciloxi)- piridin- 2- ilamina (5.8 g, 0.015 mol, 51%) como un sólido cristalino.

Ejemplo I(o):



1. 2- cloro- 3,6- diflurobenzaldehida (1.0 molar equivalente) fue disuelta en THF (0.2M) y agitada a 0°C durante 5 minutos. Se agregó la solución correspondiente cloruro de metilmagnesio (1.1 molar equivalente). La reacción fue calentada gradualmente hasta temperatura ambiente y agitada durante 2 horas. Se agregó metanol, y HCL 1N a la

mezcla y fue diluida con acetato de etilo. La mezcla fue lavada con agua, salmuera, secada sobre MgSO4, filtrada, y concentrada para proporcionar 1- (2- cloro- 3,6- difluoro- fenil)- etanol. Como un aceite. ^{1}H NMR (CDCl3 300 MHz) δ 1.42 (d, 3H), 5.21 (m , 1H), 5.42 (m, 1H), 7.09 (m, 1H), 7.18 (m, 1H).

2. 5- bromo- 3- [1- (2- cloro- 3,6- difluro- fenil)- etoxi]- piridin- 2- ilamina fue preparado siguiendo el mismo procedimiento de inicio del Ejemplo I(n) a partir de 1- (2- cloro- 3,6- difluro—fenil)- etanol y hidroxi- nitropiridina.

Ejemplo II(a): a una solución de hielo de (2,6- dicloro- fenil)- metanol (5 g, 28.2 mmol) en tetrafurano anhidro (200 mL) se agregó hidruro de sodio (1.13 g, 28.2 mmol, disponible 60%) lentamente bajo atmósfera de nitrógeno. Después de agitar durante 30 minutos, se agregó 3,5- dibromo- pirazin- 2- ilamina (7.08 g, 28.2 mmol) en tetrafurano anhidro (50 mL) a través de un embudo de adición. Una vez la adición fue completada el baño de hielo fuer removido y la reacción sometida hasta reflujo bajo nitrógeno y monitoreada mediante fase inversa de HPLC. Después de 18 horas HPLC mostró que la mayoría de 3,5- dibromo- pirazin- 2- ilamina de inicio había sido consumida y la reacción fue dejada enfriar a temperatura ambiente. La mezcla de reacción fue concentrada hasta que quedaron 50 mL. A mezcla fue diluida con acetato de etilo (200 mL) y extraída con 50% de salmuera (2 x 200 mL). La capa orgánica fue secada sobre sulfato de magnesio anhidro y concentrada al vacío. El producto crudo fue purificado utilizando una columna de gel de sílice eluyendo con 1:1 acetato de etilo/diclorometano para proporcionar 5- bromo- 3- (2,6- dicloro- benciloxi)- pirazin- 2- ilamina como un sólido de color blanco.

Ejemplo II(b): 5- bromo- 3- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- ilamina fue preparado siguiendo el procedimiento 2 a partir de (2- cloro- 3,6- difluoro- fenil)- metanol y 3,5- dibromo- pirazin- 2- ilamina.

Ejemplo II(c):

1. Se disolvió 2- cloro- 3,6- difluorobenzaldehido (1.0 molar equivalente) en THF (0.2M) y se agito a 0°C durante 5 minutos. Se agregó la correspondiente solución de cloruro de metilmagnesio (1:1 molar equivalente). La reacción fue calentada gradualmente hasta temperatura ambiente y agitada durante 2 horas se agregó metanol y HCl 1N a la mezcla y se diluyo con acetato de etilo. La mezcla fue lavada con agua, salmuera, secada sobre MgSO4, filtrada y concentrada para proporcionar 1- (2- cloro-

3,6- difluoro- fenil)- etano como aceite. ^{1}H NMR (400 MHz, DMSO- d6) δ 1.42 (d, 3H), 5.21 (m , 1H), 5.42 (m, 1H), 7.09 (m, 1H), 7.18 (m, 1H).

2. Se preparó 5- bromo- 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- ilamina siguiendo el procedimiento 2 a partir de 1- (2- cloro- 3,6- difluoro- fenil)- etanol y 3,5- dibromo- pirazin- 2- ilamina.

Ejemplo II(d):

1. Se preparó 1- (2- cloro- 3,6- difluoro- fenil)- 2- metil- propan- 1- ol siguiendo el procedimiento del ejemplo II(c) utilizando cloruro de isopropilmagnesio ^{1}H NMR (400 MHz, DMSO- d6) δ 0.63 (d, 3H), 1.06 (d , 3H), 2.19 (m, 1H), 4.59 (m, 1H), 5.54 (d, 1H), 7.21 (m, 1H), 7.36 (m, 1H).

2. se preparó 5- bromo- 3- [1- (2- cloro- 3,6- difluoro- fenil)- 2- metil- propoxi]- pirazin- 2- ilamina siguiendo el procedimiento 2 a partir del 1- (2- cloro- 3,6- difluoro- fenil)- 2- metil- propan- 1- ol y 3,5- dibromo- pirazin- 2- ilamina.

Ejemplo II(e):

1. Se agitó 2,6- dicloro- 3- fluoroacetofenona (15 g, 0.072 mol) en THF (150 mL, 0.5 M) a 0°C utilizando un baño de hielo durante 10 minutos. Se agregó hidruro de litio aliminio (de Aldrich, 2.75 g, 0.072 mol) lentamente. La reacción se agitó a temperatura ambiente durante 3 horas. La reacción se enfrió en un baño de hielo, y agua (3 mL) por goteo seguido por adición de NaOH (3 mL) lentamente. La mezcla se agitó a temperatura ambiente durante 30 minutos. Se agregó NaOH al 15% (9 mL), MgSO4 y la mezcla se filtro para remover los sólidos. Los sólidos fueron lavados con THF (50 mL) y el filtrado fue concentrado para proporcionar 1- (2,6- dicloro- 3- fluoro- fenil)- etanol (14.8 gm, rendimiento 95%) como un aceite amarillo ^{1}H NMR (400 MHz, DMSO- d6) δ 1.45 (d, 3H), 5.42 (m , 2H), 7.32 (m, 1H), 7.42 (m, 1H).

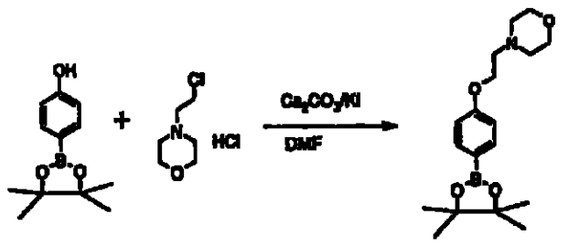
2. Se preparó 5- bromo- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- ilamina siguiendo el procedimiento 2 a partir de 1- (2,6- dicloro- 3- fluoro- fenil)- etanol y 3,5- dibromo- pirazin- 2- ilamina.

Ejemplo II- (f): Se preparó 5- bromo- 3- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- ilamina siguiendo el procedimiento 2 a partir de (3- fluoro- 2- trifluorometil- fenil)- metanol y 3,5- dibromo- pirazin- 2- ilamina.

303

Ejemplo I- 1: Una mezcla de 5- bromo- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina (Ejemplo I(a), 100 mg, 0.29 mmol), 4- (4,4,5,5- tetrametilo- 1,3- 2- dioxabordan- 2- il)- fenol (86 mg, 0.35 mmol), cloruro de bis(trifenilfosfina)- paladio (II) (8 mg, 0.009 mmol) y carbonato de sodio (91 mg, 0.87 mmol) en eter dimetilico de glicol de etileno (10 mL) y agua (0.5 mL) fue calentada hasta reflujo bajo nitrógeno durante 18 horas. La reacción fue enfriada a temperatura ambiente y diluida con acetato de etilo. La mezcla fue lavada con agua, salmuera, secada sobre Na2SO4 y purificada sobre una columna de sílice para proporcionar 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenol como cristales claros de pino (89 mg, rendimiento 85%).

Ejemplo I- 2



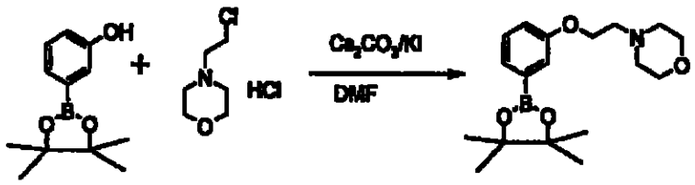
1. A una mezcla de 4- (4,4,5,5- tetrametil- 1,3- 2- dioxabordan- 2- il)- fenol (5.00 g, 22.72 mmol) y Cs2CO3 (16.29 g; 49.98 mmol) en DMF (100 mL) se agregó hidrocloruro de 4- (2- cloroetil)morfolina (4.65 g, 24.99 mmol) y KI (0.2 g, 0.6 mmol). La mezcla fue agitada a 65°C en un baño de aceite durante la noche y luego enfriada a temperatura ambiente.

La mezcla de reacción fue diluida con acetato de etilo (600 mL), y particionado con agua. La capa de agua fue extraída con acetato de etilo (2 X 50 mL). La solución combinada de acetato de etilo fue lavada con salmuera (5x100 mL), secada sobre Na2SO4, filtrada, condensada, y secada en alto vacío para proporcionar 4- {2- [4- (4,4- 5,5- tetrametil- [1,3,2]dioxaboralan- 2- il)- fenoxi]- etil}- morfina (6.8 g, rendimiento 90%) como un sólido blancuzco. ^{1}H NMR (400 MHz, DMSO- d6) δ 7.55 (d, 2H), 6.90 (d , 2H), 4.07 (t, 2H), 3.54 (m, 1H), 2.65 (t, 2H), 2.43 (m, 4H).

1. Se preparó 3- (2,6- dicloro- benciloxi)- 5- [4- (2- morfolin- 4- il etoxi9- fenil]- piridin- 2- ilamina siguiendo la preparación a partir de 5- bromo- 3- (2- dicloro- benciloxi)- piridin- 2- ilamina (ejemplo I(a) y 4- {2- [4- (4,4,5,5- tetrameti-

[1,3,2]dioxaborolan- 2- il)- fenoxi]- etil}- morfolina (preparado en parte 1) siguiendo el procedimiento 3 como un sólido de color blanco.

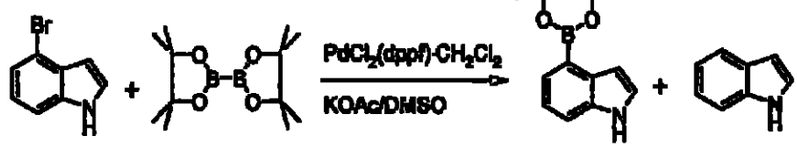
Ejemplo I- 3:



1. Se preparó 3- {2- [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenoxi]- etil}- morfolina siguiendo el mismo procedimiento como 4- {2- [4- (4,4,5,5- tetrametil- [1,3,2]dioxaboran- 2- il)- fenoxi]- etil}- morfolina en el ejemplo I- 2 utilizando 3- (4,4,5,5- tetrametil- 1,3- 2dioxabordan- 2- il)- fenol en rendimiento 92% como un solido blanco. ^{1}H NMR (400 MHz, DMSO- d6) δ 7.28 (t, 1H), 7.22 (dt , 1H), 7.14 (d, 1H), 7.04 (ddd, 1H), 4.06 (t, 2H), 3.56 (m, 4H), 2.49 (t, 2H), 2.45 (m, 4H).

2. Se preparó 3- (2,6- dicloro- benciloxi)- 5- [3- (2- morfolin- 4- iletoxi)- fenil]- piridin- 2- ilamina a partir de 5- bromo- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina (ejemplo I(a)) y 3- {2- [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenoxi]- etil}- morfolina preparado en la parte 1 siguiendo el procedimiento 3 como un sólido amarillo.

Ejemplo I- 4:



1. A un mezcla de 4- bromoindole (9.80g, 50 mmol), diborato de pinacol (13.97 g, 55 mmol), y KOAc (14.72 g, 150 mmol) en DMSO (200 mL) se agregó catalizador de paladio PdCl2(dppf)CH2Cl2 (1.22g, 1.5 mmol). El sistema fue degasificado, y luego cargado con nitrógeno tres veces. La mezcla fue agitada a temperatura ambiente a 80°C en un baño de aceite bajo nitrógeno durante 22 horas. TLC mostró la completa ausencia del material de inicio 4- bromoindol. La mezcla fue enfriada a temperatura ambiente, y luego vertida en agua (L). El producto fue extraído con acetato de etilo tres veces. Los

extractos combinados fueron lavados con salmuera cinco veces para retirar el solvente DMSO, luego secados sobre Na2SO4. Durante el paso del lavado, el catalizador puede precipitarse fuera, el cual fue removido mediante precipitación. La solución de acetato de etilo fue filtrada y condensada. El residuo fue purificado sobre una columna de gel de sílice eluyendo con EtOAc- hexano (9:1) la primera fracción proporciono el producto secundario indol (1.25g, rendimiento 21%), R*f* 0.055 (EtOAc- hexano 5:1). La segunda fracción proporciono 4- (4,4,5,5- tetrametil- [1,3,2]dioxoborolan- 2- il)- 1H- indol como un sólido blanco (8.01g,66%), R*f* 0.46 (EtOAc- hexano 5:1). ^{1}H NMR (300 MHz, DMSO- d6) δ 11.03 (bs, 1H, N- H)), 7.49 (d, J 7.7 Hz, 1H, H- 5), 7.38 (dd, J, 0.9 Hz, 1H, H- 7), 7.38 (t, J, 2.6 Hz,1H, H- 2), 7.06 (dd, J, 7.7 Hz, J 7.0 Hz, 1H, H- 6), 6.73 (bd, J 2.2 Hz, 1H, H- 3), 1.32 (s, 12H, 4CH3); Ms (m/e): 244 $(M+H)^+$.

2. Se preparó 3- (2,6- dicloro- benciloxi)- 5- (1H- indol- 4- il)- piridin- 2- ilamina a partir de 5- bromo- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina (ejemplo I(a) y 4- (4,4,5,5- tetrametil[1,3,2]dioxaborolan- 2- il) siguiendo el procedimiento 3. La primera fracción fue identificada como 3- (2,6- dicloro- benciloxi)- 5- (1H- indol- 4- il)- piridin- 2- ilamina.

Ejemplo I- 5: el mismo experimento fue realizado como el ejemplo 4, y la segunda fracción fue identificada como 3- [2- cloro- 6- (1- H- indol- 4- il)- piridin- 2- ilamina.

Ejemplo I- 6: Se preparó éster tert- butilico del ácido 2- [amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- pirrola- 1- carboxilico a partir de 5- bromo- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina (Ejemplo I(a)) y ácido N- Boc pirrola- 2- boronico siguiendo el procedimiento 3.

Ejemplo I- 7S: A una mezcla de éster tert- butilico del ácido 2- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- pirrola- 1- carboxilico (ejemplo 6, 30 mg, 0- 069 mmol) en etano/agua (2:1, 10 mL) se agregó carbonato de sodio (100 mg, 0.95 mmol). La mezcla fue sometida hasta reflujo durante la noche. La reacción fue enfriada a temperatura ambiente y extraída con acetato de etilo. La mezcla fue lavada con agua, salmuera, secada sobre Na2SO4, y purificada sobre una columna de gel de sílice para proporcionar 3- (2,6- dicloro- benciloxi)- 5- (1H- pirrol- 2- il)- piridin- 2- ilamina.

306

Ejemplos I- 8 a I- 12: Los compuestos de los ejemplos I- 18 a I- 12 fueron preparados según el procedimiento 3 utilizando 5- bromo- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina y: ácido boronico de 4- fluorofenilo (Ejemplo I- 8); ácido boronico de fenilo (Ejemplo I- 9); ácido boronico de 2- fluorofenilo (Ejemplo I- 10); ácido boronico del 3- fluorofenil (Ejemplo I- 11); y 4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenilamina (Ejemplo I- 12).

Ejemplo I- 13: A una solución de 5- (4- amino- fenil)- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina (100 mg, 0.26 mmol) en cloruro de metileno (5 mL) a 0°C, se agregó cloruro de metanosulfonilo (0.021 mL, 0.28 mmol) y 4- metilmorfina (0.16 mL). La mezcla fue agitada a temperatura ambiente durante 2 horas, y diluida con acetato de etilo. Las capas orgánicas fueron lavadas con salmuera , secadas sobre sulfato de sodio y concentradas. El residuo fue purificado con columna de gel de sílice eluyendo con acetato de hexano- etil (5:1) para proporcionar N- {4- [6- amino- 5- (2,6- dicloro- benciloxi9- piridin- 3- il]- fenil}- metanosulfonamida.

Ejemplo I- 14: A una solución de 5- (4- amino- fenil)- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina (100 mg, 0.28 mmol) en acetonitrilo (3 mL) a 0°C, se agregó piridina (0.035 mL, 1.5 eq), y anhidro acético (0.03 mL, 0.28 mmol). La mezcla fue agitada a temperatura ambiente durante la noche. Y el precipitado fue filtrado para proporcionar N- {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- acetamida como un sólido blanco.

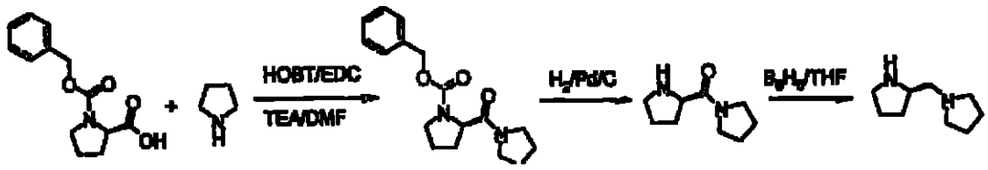
Ejemplo I- 15 a I- 35: Los compuestos de los ejemplos I- 15 a I- 35 fueron preparados según el procedimiento 3 a partir de 5- bromo- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina y: 3- (4,4,5,5- tetrametil- [1,3,2]dioxoborolan- 2- il)- fenol (ejemplo I- 15); ácido boronico de 4- metoxifenilo (ejemplo I- 16); ácido 3- aminobencenoboronico (Ejemplo I- 17); ácido 4- trifluorometoxibencenoboronico (Ejemplo I- 18); ácido boronico de 2- hidroxibenceno (ejemplo I- 19); - ácido 2- fenoxifenilboronico (Ejemplo I- 20); ; ácido 3,4- difluorofenilboronico (Ejemplo I- 21); ácido (3- isopropil)fenilboronico (ejemplo I- 22); ácido (2- trifluorometilfenil)boronico (Ejemplo I- 25); ácido [(2- metilsulfonilamino)fenil]boronico (Ejemplo I- 26); ácido 4- hidroximetilfenilboronico (Ejemplo I- 27); ácido 3,4- metilenodioxofenilboronico

(Ejemplo I- 28); ácido 2- trifluorometoxifenilboronico (Ejemplo I- 29); ácido 4- metiltiofeno- 2- boronico (Ejemplo I- 30); ácido 2- benciloxifenilboronico (Ejemplo I- 31); ácido 3- metoxifenilboronico (Ejemplo I- 32); ácido 1- (tert- butoxicarbonil)indol- 2- boronico y el grupo tert- butoxicarbonilo fue retirado utilizando el 20% de ácido trifluoroacetico en diclorometano (Ejemplo I- 33); ácido (3- fluoro- 4- benciloxifenil)boronico (Ejemplo I- 34); y ácido 4- (4,4,5,5- tetrametil- [1,3,2]dioxoborolan- 2- il)- benzoico (Ejemplo I- 35).

Ejemplo I- 36: A una solución de ácido 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- benzoico (50 mg, 0.13 mmol), HOBT (21 mg, 0.156 mmol), y EDC (30 mg, o.156 mmol), y EDC (30 Mg, mmol) en DMF (2 mL) se agregó N, N- dietiletilenodiamina (0.022 mL, o.156 mmol). La reacción fue agitada a temperatura ambiente durante 24 horas, luego diluida con EtOAc, y particionado con H2O. La capa orgánica fue separada y la capa acuosa fue extraída con EtOAc. Las capas orgánicas fueron combinadas, lavadas con NaHCO3 saturado, y concentradas hasta sequedad al vacío. El material fue purificado utilizando cromatografía de columna (sílice gel, 99:1 a 95:5 Ch2Cl2/MeOH) para proporcionar 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- N- (2- dietilamino- etil)- benzamida (45 mg, rendimiento 72%) como un sólido blanco.

Ejemplos I- 37 y I- 38: Los compuestos de los ejemplos I- 38 fueron preparados a partir del ácido 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- benzoico y N, N- dietil- 1,3- propanediamina (Ejemplo I- 37) y 1- metilpiperazina (Ejemplo I- 38), siguiendo el procedimiento 4.

Ejemplo I- 39



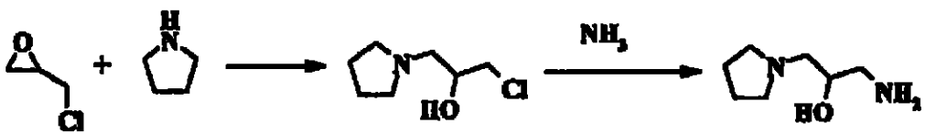
1. Una mezcla de (+)carbobenciloxi- D- prolina (1.5 g, 6 mmol), EDC (2.3 g, 12 mmol), HOBt (800 mg, 6 mmol), TEA (1.5 mL) y pirrolidina (853 mg, 12 mmol) en DMF (20 mL) fue agitada a temperatura ambiente durante 18 horas. La reacción fue diluida con agua y bicarbonato de sodio, extraida con diclorometano (3X). El DMC combinado fue concentrado y purificado sobre una columna de gel de sílice para

proporcionar éster bencilico del ácido (R)- 2- (pirrolidina- 1- carbonil)- pirrolidina- 1- carboxilico. El éster bencilico del ácido (R)- 2- (pirrolidina- 1- carbonil)- pirrolidina- 1- carboxilico fue hidrogenada utilizando Pd/c en metanol a temperatura ambiente durante 20 horas para proporcionar pirrolidin- 1- il- (R)- pirrolidin- 2- il- metanona. A un solución de pirrolidin- 1- il- (R)- pirrolidin- 2- il- metanona (1.2 g, 7.1 mmol) en THF (10 mL) a 0°C se agregó B2H6 (10 mL, 10 mmol). La mezcla fue calentada hasta reflujo durante 16 horas. La reacción fue acidificada con HCl y concentrada. El residuo fue basificado a pH 10 con NaOH 2N y extraída con metanol al 5% en DCM. La capa orgánica fue concentrada y purificada sobre columna de gel de sílice para proporcionar 800 mg (73%) de (R)- 2- pirrolidin- 1- ilmetil- pirrolidina.

2. Se preparó {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona a partir del ácido 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- benzoico y (2R)- 2- pirrolidin- 1- ilmetil- pirrolidina siguiendo el procedimiento 4.

Ejemplos I- 40 a I- 45: las compuestos de los Ejemplos I- 40 a I- 45 fueron preparados según el procedimiento 4 a partir del 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- benzoico y: (2S)- 2- pirrolidin- 1- metil- pirrolidina (Ejemplo I- 40); 4- pirrolidin- 1- il- piperidina (Ejemplo I- 41); 4- piperidina- etanol (Ejemplo I- 42); (3S)- (3- dimetilamino- pirrolidina (Ejemplo I- 43); (3R)- (3- dimetilamino- pirrolidina (Ejemplo I- 44); y (S)- 3- ciclopropilaminometil- piperidina (preparado según los procedimientos para (R)- 2- pirrolidin- 1- ilmetil- pirrolidina en ejemplo I- 39) (Ejemplo I- 45).

Ejemplo I- 46:



1.A una solución de epiclohidrin (de Aldrich, Milwaukee, 3.91 mL, 50.0 mmol) en EtOH (100 mL) se agregó pirrolidina (4.18 mL, 50.0 mmol) a temperatura ambiente. La mezcla fue agitada a 55-60°C durante 20 horas, luego sometida has reflujo durante 3 horas. El solvente fue removido bajo presión reducida y 1- cloro- 3- pirrolidin- 1- il- propan- 2- ol crudo fue obtenido como un aceite (10 g). Este producto aceitoso fue disuelto en amoniaco 7M en MeOH (40 mL) y fue agitado a temperatura ambiente

durante la noche. Luego se agregaron otros 30 mL de amoniaco 7M en MeOH y la mezcla fue agitada a 40°C durante la noche. NMR mostró que el material de inicio desaparecido completamente. El solvente fue removido y el residuo fue disuelto en HCl 2N y luego liofilizado para proporcionar 10.8 g de producto de aceite sal, el cual fue disuelto en MeOHH2O a 0°C y la resina (AG1 x 8, en forma de hidroxido) se agregó en porciones con agitación hasta que el pH de la solución es 9.0 aproximadamente. Después de filtración, el filtrado fue evaporado bajo presión reducida para proporcionar la amina libre 1- amino- 3- pirrolidin- 1- il- propan- 2- ol como un aceite amarillento (8.6 g). Este producto crudo fue utilizado para la reacción sin purificación adicional.

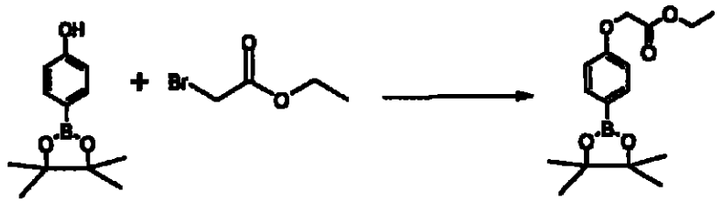
1. Se preparó 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- N- (2- hidroxi- 3- pirrolidin- 1- il- propil)- benzamida a partir del ácido 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- benzoico y 1- amino- 3- pirrolidin- 1- il- propan- 2- ol siguiendo el procedimiento 4.

Ejemplos I- 47 a I- 52: los compuestos de los Ejemplos I- 47 a I- 52 fueron preparados según el procedimiento 4 a partir del 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- benzoico y: 3- fluoro- 1- (2S)- pirrolidin- 1- metil- piperidina (preparada según los procedimientos para (R)- 2- pirrolidin- 1- ilmetil- pirrolidina) (Ejemplo I- 47); 1- ciclopropil- piperazina (Ejemplo I- 48); (R)- 2- [(ciclopropilmetil- amino)- metil]- pirrolidina (preparada según los procedimientos para (R)- 2- pirrolidin- 1- ilmetil- pirrolidina) (primera fracción, Ejemplo I- 49; segunda fracción Ejemplo I- 50); N- y (2- hidroxi- 3- pirrolidin- 1- il- propil)- N- metil- amina (preparado según el mismo procedimiento como 1- amino- 3- pirrolidin- 1- il- propan- 2- ol (Ejemplo I- 51) y (2S)- 2- [(3R)- 3- hidroxi- pirrolidin- 1- ilmetil)- pirrolidina (preparada según el procedimiento para (R)- 2- pirrolidin- 1- ilmetil- pirrplidina) (Ejemplo I- 52).

Ejemplo I- 53: Se preparó ácido 3- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- benzoico a partir de 5- bromo- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina y 3- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- benzoico siguiendo el procedimiento 3.

Ejemplo I- 54: Se preparó {3- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona a partir del ácido 3- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- benzoico y (R)- 2- pirrolidin- 1- ilmetil- pirrolidina siguiendo el procedimiento 4.

Ejemplo I- 55



1. A una solución de 4- (4,4,5,5- tetrametil- [1,3]- fenol (10.0 g, 45.5 mmol) y Cs2CO3 (23.5 g, 68.25 mmol) en DMF (60 mL) se agregó α- bromoacetato (11.6 g, 68.25 mmol). La mezcla fue agitada a temperatura ambiente durante 24 horas, luego diluida con acetato de etilo, lavada con agua, secada sobre Na2SO4.después de filtración y evaporación, el residuo fue secado al vacío para proporcionar éster etilico del ácido [4- (4,4,5,5- tetrametil- [1,3]dioxolan- 2- il)- fenoxi]acetico (12.52 g, rendimiento90%) como un aceite.

2. Una mezcla de 5- bromo- 3- (2,6- dicloro- benciloxi)- piridin –2- ilamina (ejemplo I(a)) (2.2 g, 6.3 mmol), éster etilico del ácido 4[4- (4,4,5,5- tetrametil – [1,3]dioxolan- 2- il)- fenoxi]- acetico 82.9, 1.5 eq.), cloruro bis(trifenilfosfina)paladio(II) (136 mg) y carbonato de sodio (1.93 g, 3.0 eq.) en éter dimetilico de glicol de etileno (30 mL), DMF (5 mL) y agua (8 mL) se calentó a 90-100°C bajo nitrógeno durante 7 horas. La reacción fue enfriada a temperatura ambiente y diluida con acetato de etilo. La mezcla fue lavada con agua, salmuera, secada y purificada sobre una columna de sílice para proporcionar éster etilico del ácido {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]fenoxi}- acetico. Este éster fue tratado con carbonato de sodio y agua a temperatura ambiente durante la noche. La reacción fue diluida con acetato de etilo. La mezcla fue lavada con agua, salmuera, secada y purificada para proporcionar ácido 4- [6- amino- 5- (2,6- dicloro- benciloxi9- piridin- 3- il]- fenoxi}- acetico.

Ejemplo I- 56: Se preparó 2- {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenoxi}- 1- [(2R)- 2- pirrolidin - 1- il]- etanona a partir del ácido 4[6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenoxi}- acetico y (R)- 2- pirrolidin- 1- ilmetil- pirrolidina siguiendo el procedimiento 4.

Ejemplo I- 57: Se preparó 2- {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenoxi}- 1- [(2S)- 2- pirrolidin - 1- ilmetil- pirrolidin- 1- il]- etanona a partir del ácido 4[6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenoxi}- acetico y (S)- 2- pirrolidin- 1- ilmetil- pirrolidina siguiendo el procedimiento 4.

Ejemplo I- 58: Se preparó 3- (2,6- dicloro- benciloxi)- 5- (1H- indol- 5- il)- piridin- 2- ilamina a partir del ácido 5- bromo- (2,6- dicloro- benciloxi)- piridin- 2- ilamina y ácido indol- 5- boronico siguiendo el procedimiento 3.

Ejemplo I- 59: A una solución de 3- (2,6- dicloro- benciloxi)- 5- (1H- indol- 5- il)- piridin- 2- ilamina (ejemplo I- 58, 200mg, 0.52 mmol) en ácido acetico (4 mL) y ácido trifluoroacetico (1 mL) se agregó 1- metil- 4- piperidona (0.32 mL, 2,6 mmol). La solución fue sometida hasta reflujo durante la noche, y evaporada. El residuo fue disuelto en acetato de etilo, lavado con NaHCO3 saturado y salmuera, secado sobre NaSO4 y concentrado. El producto crudo fue purificado sobre una columna de gel de sílice eluyendo con diclorometano- metanol- trietilamina (95:5:0.1) para proporcionar3- (2,6- dicloro- benciloxi)- 5- [3- (1- metil- 1,2,3,6- tetrahidro- piridin- 4- il)- 1H- indol- 5- il]- piridin- 2- ilamina (103.5 mg rendimiento 41%) como un sólido cristalino de color naranja.

Ejemplo I- 60: A una solución degasificada de 3- (2,6- dicloro- benciloxi)- 5- [3- (1- metil- 1,2,3,6- tetrahidro- piridin- 4- il)- 1H- indol- 5- il]- piridin- 2- ilamina (ejemplo I- 61, 130 mg, 0.27 mmol) en metanol (50 mL) y ácido acetico (5 mL) se agregó Pd/C al 10% (50 mg). La solución fue degasificada y cargada con hidrogeno durante tres veces, y luego fue agitada bajo un globo de hidrogeno durante la noche. La mezcla fue filtrada a través de un cojín de Celite, lavada con metanol, y luego condensada. El residuo fue disuelto en acetato de etilo, lavado con NaCO3 saturado y salmuera, secada sobre Na2SO4 y condensada. El producto crudo fue purificado sobre una columna de gel de sílice eluyendo con diclorometano- metanol- trietil- amina (95:5:01) para proporcionar 3- (2,6- dicloro- benciloxi)- 5- [3- (1- metil- piperidin- 4- il)- 1H- indol- 5- il]- piridin- 2- ilamina como un sólido blanco.

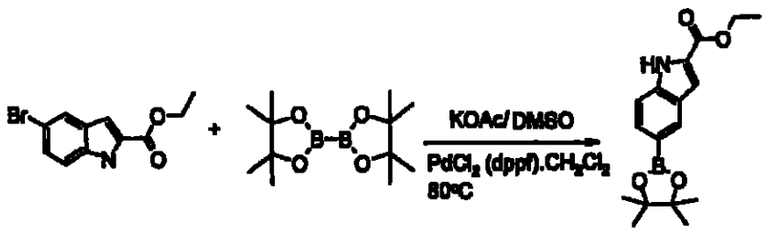
Ejemplos I- 61 a I- 68: los compuestos de los Ejemplos I- 61 a I- 68 fueron preparados según el procedimiento 4 a partir de 3- (2,6- dicloro- benciloxi)- 5- (1H-

indol- 5- il)- piridin- 2- ilamina y: morfolina (Ejemplo I- 61); piperidina (Ejemplo I- 62); pirrolidina (Ejemplo I- 63); dietilamina (Ejemplo I- 64); éster tert- butilico del ácido pirrolidin- 3- il- carbamico (Ejemplo I- 65); 2,6- dimetil- morfolina siguiendo (Ejemplo I- 66); y (R)- pirrolidin- 3- il- acetamida (Ejemplo I- 67); y piperazin- 1- il- etanona (Ejemplo I- 68).

Ejemplo I- 69: Se preparó 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (1H- indol- 5- il)- piridin- 2- ilamina a partir de 5- bromo- 3- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 2- ilamina y ácido indol- 5- boronico siguiendo el procedimiento 3.

Ejemplos I- 70 a I- 75: los compuestos de los Ejemplos I- 70 a I- 75 fueron preparados según el procedimiento 5 a partir de 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (1H- indol- 5- il)- piridin- 2- ilamina y: piperazin- 1- il- metanona (Ejemplo I- 70); 2,6- dimetil- morfina (Ejemplo I- 71); (3S)- pirrolidin- 3- il- acetamida (Ejemplo I- 72); piperidina (Ejemplo I- 73); morfina (Ejemplo I- 74); y pirrolidina (Ejemplo I- 75).

Ejemplo I- 76



1. A una solución agitada de 5- bromo- 1H- indol- 2- carboxilato (5g, 18.6 mmol) en DMSO (75 mL, 0.25M), se agregó 4,4,4',5,5,5'- octametil- 2- 2'- bi- dioxoborolano (11.2g, 44.3 mmol), acetato de potasio (5.5 g, 56.0 mmol), y [bis(difenilfosfina)ferroceno]dicloropaladio II (1.23mmol). La mezcla fue degasificada y cargada con nitrógeno tres veces, y luego calentada a 80°C bajo nitrógeno durante la noche. La reacción fue enfriada a temperatura ambiente y diluida con acetato de etilo (2 x 100 mL). La mezcla fue lavada con agua (1x50 mL), salmuera (1x50 mL), secada sobre MgSO4 y purificado sobre una columna de gel de sílice para proporcionar 5- (4,4,5,5- tetrametil- 1,3,2- dioxaborolon- 2il)- 1H- indol- 2- carboxilito de etilo como un sólido blancuzco. ^{1}H NMR (400 MHz, DMSO- d6) δ 1.31 (t, 3H)), 4.32 (m, 2H),

7.18 (s, 1H), 7.42 (d, 1H,), 7.54 (d, 1H), 8.05 (s, 1H), 11.96 (s, 1H); Ms (m/e): 315G (M+H).

2. Se preparó éster etilico del ácido 5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carboxilico a partir de 5- bromo- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina y éster etilico del ácido 5- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- 1- indol- 2- carboxilico siguiendo el procedimiento 3.

Ejemplo I- 77: A una mezcla de 5- {6- amino- 5- [(2,6- diclorobencil)- oxi]- piridin- 3- il}- 1H- indol- 2- carboxilato de etilo (2.5 g, 5.5 mmol) en dicloro:agua (60 ml:20mL), se agregó hidroxido de litio (0.65g, 27.1 mmol). La reacción fue calentada hasta reflujo durante la noche. Mayoría del solvente fue evaporado y la mezcla fue acidificada, y agitada durante 10 minutos. El precipitado fue filtrado y lavado con agua para proporcionar 5- {6- amino- 5- [(2,6- diclorobencil)- oxi]- piridin- 3- il}- 1H- indol- 2- carboxilato como un solido de color canela.

Ejemplos I- 78 a I- 85: los compuestos de los Ejemplos I- 78 a I- 85 fueron preparados según el procedimiento 4 a partir del ácido 5- [6- amino- 5- (2,6- benciloxi)- piridin- 3- il]- 1H- indol- 2- carboxilico y N- metil- piperazina (Ejemplo I- 78); (3R)- 3- dimetilamino- pirrolidina (Ejemplo I- 79); (2R)- pirrolidin- 1- ilmetil- pirrolidina (preparada como en el Ejemplo I- 39) (Ejemplo I- 80); 2- pirrolidin- 1- etilamina (Ejemplo I- 81); 2- morfolin- 4- il- etilamina (Ejemplo I- 82); éster tert- butilico del ácido (S)- pirrolidin- 3- il- carbamico (Ejemplo I- 83), seguido por desprotección del grupo BoC en ácido trifluoroacetico al 20% en diclorometano (Ejemplo I- 84); 2- hidroxi- 3- pirrolidin- 1- il- propilamina (Ejemplo I- 85).

Ejemplo I- 86: Se preparó 4- (6- amino- 5- benciloxi- piridin- 3- il)- fenol a partir de 3- benciloxi- 5- bromo- piridin- 2- ilamina y 4- (4,4,5,5- tetrametil- 1,3- 2- dioxabordan- 2- il)- fenol siguiendo el procedimiento 3.

Ejemplo I- 88: Se preparó 3- (3- metoxi- benciloxi)- 5- fenil- piridin- 2- ilamina según el procedimiento 6.

Ejemplos I- 89 a I- 105: Los compuestos de los ejemplos I- 89 a I- 105 fueron preparados según el procedimiento 6 a partir de 2- cloro- 4- fluorobencilbrumuro

(Ejemplo I- 89); 2- clorobencilbromuro (Ejemplo I- 9o); 2,5- diclorobencilbromuro (Ejemplo I- 91); 2- cloro- 5- trifluorometil- bencilbromuro (Ejemplo I- 92); 2,4- dicloro- 5- fluoro- bencilbromuro (Ejemplo I- 93); 2- cloro- 3- trifluorometil- bencilbromuro (Ejemplo I- 94); 2- cloro- 3,6- difluoro- bencilbromuro (Ejemplo I- 95); 3,4- dicloro- bencilbromuro (Ejemplo I- 96); 2- bromometil- benzonitrilo (Ejemplo I- 97); 2- cloro- 6- fluoro- 3- metil- bencilbromurro (Ejemplo I- 98); 2- bromometil- 1,3,4- trifluoro- benceno (Ejemplo I- 99); 2- bromometil- 1,3- difluoro- benceno (Ejemplo I- 100); 2- bromometil- 1,3- difluoro- 4- metil- benceno (Ejemplo I- 101);2- bromometil- 4- cloro- 1,3- difluoro- benceno (Ejemplo I- 102); 2- bromometil- 1- cloro- 3- fluoro- benceno (Ejemplo I- 103); 4- bromometil- 2- fluoro- 1- metoxi- benceno (Ejemplo I- 104) y 1- bromometil- 3- nitro- benceno seguido por reducción del grupo nitro a amino y la reacción con cloruro de metanosulfonilo (Ejemplo I- 105).

Ejemplo I- 106: Se sintetizó 5- [4- (2- morfin- 4- il- etoxi)- fenil]- 3- (3- nitrobenciloxi)- piridin- 2- ilamina según el procedimiento 7.

Ejemplos I- 107 a I- 110: Los compuestos de los ejemplos I- 107 a I- 110 fueron preparadas según el procedimiento 7 a partir de 1- bromometil- naftaleno (Ejemplo I- 107); 2- brometil- 3- cloro- 1,4- difluoro- benceno (Ejemplo I- 108); 2- bromo- N- (4- isopropil- fenil)- 2- fenil- acetamida (Ejemplo I- 109); y 3- bromometil- 5- benzo[b]tiofeno (Ejemplo I- 110).

Ejemplo I- 111: Se sintetizó {4- [6- amino- 5- (4- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 2- il]- metanona según el procedimiento 8.

Ejemplos I- 112 a I- 117: Los compuestos de los ejemplos I- 112 a I- 117 fueron preparados según el procedimiento 8 a partir de 1- bromometil- 1- fluoro- 3- trifluorometil- benceno (Ejemplo I- 112); 2- bromometil- 4- fluoro- 1- trifluorometil- benceno (Ejemplo I- 113); 1- (1- bromo- etil)- 2- trifluorometil- benceno. (Ejemplo I- 114); y 1- bromo- 2- bromometil- benceno. (Ejemplo I- 115); 1- bromometil- 3- fluoro- 2- trifluorometil- benceno (Ejemplo I- 116); y 2- bromometil- 3- cloro- 1,4- difluoro- benceno (Ejemplo I- 17).

Ejemplos I- 118 a I- 121: Los compuestos de los ejemplos I- 118 a I- 121 fueron preparados según el procedimiento 8 a partir de 5- bromo- 3- (2,6- difluoro- benciloxi)- piridin- 2- ilamina y; 4- (4,4,5,5- tetrametil- [1,3]dioxolan- 2- il)- fenol (Ejemplo I- 118); 4- {2- [4- (4,4,5,5- tetrametil- [1,3,2]dioxolan- 2- il)- fenoxi]- etil}- morfina (Ejemplo I- 119); 4- (4,4,5,5- tetrametil- [1,3]dioxolan- 2- il)- 1H- indol. (Ejemplo I- 120); y ácido 4- (4,4,5,5- tetrametil- [1,3]dioxolan- 2- il)- benzoico. (Ejemplo I- 121).

Ejemplo I- 122: Se preparó {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona a partir del ácido {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- benzoico y (2R)- 2- pirrolidin- 1- ilmetil- pirrolidina según el procedimiento 4.

Ejemplo I- 123: Se preparó {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona a partir del ácido {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- benzoico y (2S)- 2- pirrolidin- 1- ilmetil- pirrolidina siguiendo el procedimiento 4.

Ejemplo I- 124: Se preparó éster etilico del ácido {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenoxi}- acetico a partir del ácido 5- bromo- 3- (2,6- difluoro- benciloxi)- piridin- 2- ilamina y éster etilico del ácido[4- (4,4,5,5- tetrametil- [1,3]dioxolan- 2- il)- fenoxi]- acetico siguiendo el procedimiento 3.

Ejemplo I- 125: Se trató éster etilico del ácido{4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenoxi}- acetico con bicarbonato de sodio (1.28g, 12.05 mmol) y agua (10 mL) a 90- 1001C durante la noche. La reacción fue enfriada a temperatura ambiente y diluida con acetato de etilo. La mezcla fue lavada con agua, salmuera, secada y purificada sobre una columna de gel de sílice para proporcionar ácido {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenoxi}- acetico.

Ejemplo I- 126: Se preparó 2- {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- 1- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- etanona a partir del ácido {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenoxi}- acetico y (2R)- 2- pirrolidin- 1- ilmetil- pirrolidina siguiendo el procedimiento 4.

376

Ejemplo I- 127: Se preparó 2- {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenoxi}- 1- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- etanona a partir del ácido {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenoxi}- acetico y (2S)- 2- pirrolidin- 1- ilmetil- pirrolidina siguiendo el procedimiento 4.

Ejemplos I- 128 a I- 134: Los compuestos de los ejemplos I- 128 a I- 134 se prepararon según el procedimiento de 4- (4,4,5,5,- tetrameil- [1,3]dioxolan- 2- il)- fenol y: 5- bromo- 3- (2- cloro- 6- fluoro- benciloxi)- piridin- 2- ilamina (Ejemplo I- 128); 5- bromo- 3- (2- cloro- 4- fluoro- benciloxi)- piridin- 2- ilamina (Ejemplo I- 129); 5- bromo- 3- (2,4- dicloro- benciloxi)- piridin- 2- ilamina (Ejemplo I- 130); 2- (2- amino- 5- bromo- piridin- 3- iloximetil)- benzonitrilo (Ejemplo I- 131); 5- bromo- 3- (2- trifluorometil- benciloxi)- piridin- 2- ilamina (ejemplo I- 132); 5- bromo- 3- (2- cloro- benciloxi)- piridin- 2- ilamina (Ejemplo I- 133); y 5- bromo- 3- (e- tert- butil- benciloxi)- piridin- 2- ilamina (Ejemplo I- 134).

Ejemplo I- 135



1. A una solución de 4- (4,4,5,5- tetrametil- [1,3,2]dioxoborlan- 2- il)- fenilamina (5.00 g, 22.8 mmol) en cloruro de metileno (100 mL) y 4- metilmorfolina (16 mL) a 0°C se agregó cloruro de metanosulfonilo (2.1, 28 mmol). La mezcla fue agitada a temperatura ambiente durante 2 horas, y diluida con acetato de etilo. La capa orgánica fue lavada con salmuera, secada sobre sulfato de sodio y concentrada para proporcionar *N*- [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il]- metanosulfonamida como un sólido blanco (6.32 g, rendimiento del 93%). MS m/z 298 (M+1).

2. *N*- {4- [6- amino- 5- (2- ciano- benciloxi)- piridin- 3- il]- fenil}- metanosulfonamida se preparó siguiendo el procedimiento 3 a partir de 2- (2- amino- 5- bromo- piridin- 3- iloximetil)- benzonitrilo y N- [4- (4,4,5,5- tetrametil[1,3,2]dioxoborolan- 2- il)- fenil]- metanosulfonamida (Ejemplo I- 135, 650 mg, 1.65 mmol) en glicol de etileno (55 mL).

La mezcla fue calentada a reflujo y se dejo agitar durante 24 horas. La reacción fue enfriada a temperatura ambiente. La mayoría del solvente fue evaporado y la mezcla fue acidificada. El sólido precipitado fue filtrado para proporcionar ácido 2- [2- amino- 5- (4- metanosulfonilamino- fenil)- piridin- 3- iloximetil- benzóico como un sólido marrón claro. El filtrado fue neutralizado y extraido con EtOAc (5 x 20 mL). La capa orgánica fue combinada, secada sobre MgSO4, y concentrada para proporcionar 2- [2- amino- 5- (4- metanosulfonilamino- fenil)- piridin- 3- iloximetil]- benzamida como un sólido blancuzco.

Ejemplo I- 137: se preparó ácido 2- [2- amino- 5- (4- metanosulfonilamino- fenil)- piridin- 3- iloximetil]- benzóico como en el Ejemplo I- 136.

Ejemplo I- 138- 140: Los compuestos de los Ejemplos I- 138 a I- 140 fueron preparados según el procedimiento 4 a partir de ácido 2- [2- amino- 5- (4- metanosulfonilamino- fenil)- piridin- 3- iloximetil]- benzóico y: N- metil- piperazina (Ejemplo I- 138); 2- hidroxietilamina (Ejemplo I- 139); e isobutilamina (Ejemplo I- 140).

Ejemplo I- 141: 5- Bromo- 3- (2- cloro- 6- fluoro- benciloxi)- piridin- 2- ilamina (Ejemplo I(e), 9.00 g, 27.0 mmol), ácido 4- carboxibencenoborónico (4.41 g, 27.0 mmol), tetrakis(trifenilfosfina)paladio (0) (0.99 g, 0.9 mmol), carbonato de potasio (13.1 g, 95.0 mmol), dimetilformamida (72 mL) y agua (36 mL) fueron cargados en una matriz de fondo redondo de tres cuellos equipado con un termómetro, un condensador de reflujo y agitación magnética. La mezcla fue purgada con nitrogeno y gradualmente se calentó desde 81°C hasta 98°C durante un periodo de 4 horas. La cromatografía de capa delgada (acetato de etilo: hexano:ácido acetico 4:6:0.5) mostró un rastro de material de inicio a Rf 0.7, producto a Rf 0.4 y muchas impurezas pequeñas. La mezcla fue enfriada a 45°C. Los sólidos fueron recolectaods mediante filtración al vacío, lavados con 30 mL de etanol:agua 1:1 y descartados. El filtrado fue diluido con 432 mL de agua y 8 mL de solución de hidroxido de potasio 9 N (a pH 12- 13), enfriado en un baño de hielo y agitado durante 30 minutos. Los sólidos fueron recolectados mediante filtración al vacío y lavados con 5 mL de agua. El filtrado fue enfriado en un baño de hielo y acidificado a pH 7.5 con ácido acético utilizando un medidor de pH. Los sólidos fueron recolectados mediante filtración al vacío, lavados con 10 mL de etanol:agua 1:1

y secados al vacío para proporcionar 2.5 g de ácido 4- [6—amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- benzóico y un segundo compuesto como un sólido marrón en una proporción de 1:1 mediante ^{1}H- NMR. Este material fue descartado. El filtrado fue acidificado a pH 6.5 con ácido acético utilizando un medidor de pH. Los sólidos fueron recolectados mediante filtración al vacío, lavados con 10 mL de etanol:agua 1:1 y secados al vacío para proporcionar 3.6 g (rendimiento de 36%) de ácido 4- [6—amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- benzóico como un sólido marrón conteniendo una impureza de 5- 10% mediante ^{1}H- NMR.

Ejemplos I- 142 a I- 149: Los compuestos de los ejemplos I- 142 a I- 149 fueron preparados según el procedimiento 4 a partir del ácido 4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- benzóico y: (2R)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo 1- 142); (2S)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo I- 143); (3S)- 3- dimetilamino- pirrolidina (Ejemplo I- 144); éster tert- butílico del ácido (S)- pirrolidin- 3- il- carbámico, seguido por desprotección del grupo Boc con ácido trifluoroacético en diclorometano (Ejemplo I- 145); N- metilpiperazina (Ejemplo I- 146); 1- piperazin- 1- il- etanona (Ejemplo I- 147); 2- morfolin- 4- il- etilamina (Ejemplo I- 148); 3- morfolin- 4- il- propilamina (Ejemplo I- 149).

Ejemplo I- 150: 5- Bromo- 3- (2- cloro- benciloxi)- piridin- 2- ilamina (4.50 g, 14.3 mmol), ácido carboxibencenoborónico (2.62 g, 15.8 mmol), tetrakis(trifenilfosfina)paladio(0) (0.56 g, 0.5 mmol), carbonato de potasio (6.90 g, 50 mmol), dimetilformamida (36 mL), y agua (18 mL) fueron cargados en una matraz de fondo redondo de 3 cuellos de 250 mL equipada con un termómetro, condensador de reflujo y agitación magnética. La mezcla fue purgada con nitrogeno y gradualmente calentada de 82 a 93°C durante un periodo de 4 horas. La cromatografía de capa delgada (acetato de etilo:hexano:ácido acético 4:6:0.5) mostró producto a Rf 0.3 y pocas impurezas pequeñas. La mezcla fue enfriada a 45°C. Los sólidos fueron recolectados mediante filtración al vacío, lavados con 10 mL de etanol:agua 1:1 y descartados. El filtrado combinado fue diluido con 216 mL de agua y 4 mL de solución de hidroxido de potasio 9N (a pH 12- 13), enfriado en un baño de hielo y agitado durante 30 minutos con 3 g de Celite y 3 g de Norit. Los sólidos fueron recolectados mediante filtración al vacío a través de un cojin de Celite y lavados con 10 mL de agua. Los sólidos fueron descartados. El filtrado combinado fue enfriado en un baño de hielo y acidificado a pH

7 con ácido acético utilizando un medidor de pH. Los sólidos fueron recolectados mediante filtración la vacío, lavados con 20 mL de etanol:agua 1:1 y secados al vacío para proporcionar 2.7 g (rendimiento de 53%) del ácido 4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]benzóico.

Ejemplos I- 151 a I- 159: Los compuestos de los Ejemplos 1- 151 a 1- 159 fueron preparados según el procedimiento 4 a partir del ácido 4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]benzóico y: (2R)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo I- 151); (2S)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo I- 152); (3S)- 3- dimetilamino- pirrolidina (Ejemplo I- 153); éster tert- butílico del ácido pirrodilin- 3- il- carbámico, seguido por desprotección del grupo Boc con ácido trifluoroacético en diclorometano (Ejemplo I- 154); 4- pirrolidin- 1- il- piperidina (Ejemplo I- 155); N- metilpiperzina (Ejemplo I- 156); 1- piperazin- 1- il- etanona (Ejemplo I- 157); 2- morfolin- 4- il- etilamina (Ejemplo I- 158); y 3- morfolin- 4- il- propilamina (Ejemplo I- 159).

Ejemplo I- 160: 2- (2- amino- 5- bromo- piridin- 3- iloximetil)- benzonitrilo (9.0 gm 29.6 mmol), ácido carboxibencenoborónico (5.4 g, 32.5 mmol), tetrakis(trifenilfosfina)paladio(0) (1,1 g, 1.0 mmol), carbonato de potasio anhidro (13.8 g, 70.0 mmol), dimetilformamida (72 mL) y agua (36 mL) fueron cargados en una matraz de fondo redondo de tres cuellos equipada con un termómetro, un condensador de reflujo y agitación magnética. La mezcla fue purgada con nitrogeno y gradualmente calentada desde 81 a 90°C durante un periodo de 2 horas. La cromatografía de capa delgada (acetato de etilo:hexano:ácido acético 4:6:0.5) mostró un rastro de material de inicio a Rf 0.7, producto a Rf 0.4 y una impureza a Rf 0.5. La mezcla fue enfriada a 45°C. Los sólidos viscosos fueron recolectados mediante filtración al vacío, lavados con 30 mL de etanol:agua 1:1 y descartados. El filtrado fue diluido con 432 mL de agua y 8 mL de solución de hidroxido de potasio (a pH 12- 13), enfriados en un baño de hielo y agitados durante 3 minutos. Los sólidos fueron recolectados mediante filtración al vacío y lavados con 20 mL de agua. Los solidos fueron descartados. El filtrado fue enfriado en un baño de hielo acidificado con ácido acético a pH 7.5 utilizando un medidor de pH. Los sólidos fueron recolectados mediante filtración al vacío, lavados con 20 mL de agua y secados al vacío para proporcionar 8.5 g(rendimiento de 83%) de ácido 4- [6- amino- 5- (2- ciano- benciloxi)- piridin- 3- il]benzóico como un sólido muy oscuro.

320

Ejemplos I- 161 a I- 170: Los compuestos de los ejemplos I- 161 a I- 170 se prepararon según el procedimiento 4 a partir del ácido 4- [6- amino- 5- (2- ciano- benciloxi)- piridin- 3- il]- benzóico y: (2R)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo I- 161); (2R)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo I- 162); (3S)- 3- dimetilamino- pirrolidina (Ejemplo I- 161); (2R)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo I- 162); (3S)- 3- dimetilamino- pirrolidina (Ejemplo I- 163); éster tert- butílico del ácido (S)- pirrolidin- 3- il- carbámico, seguido por desprotección del grupo Boc con ácido trifluoroacético en diclorometano (Ejemplo I- 164); 4- pirrolidin- 1- il- piperidina (Ejemplo I- 165); N- metilpiperazina (ejemplo I- 166); 1- piperazin- 1- il- etanona (Ejemplo I- 167); 1- metil- piperidin- 4- ilamina (Ejemplo I- 166); 1- piperazin- 1- il- etanona (Ejemplo I- 167); 1- metil- piperidin- 4- ilamina (Ejemplo I- 168); 2- morfolin- 4- il- etilamina (Ejemplo I- 169); y 3- morfolin- 4- il- propilamina (Ejemplo I- 170).

Ejemplo I- 171: 5- Bromo- 3- (2,4- dicloro- benciloxi)- piridin- 2- ilamina (6.96 g, 20.0 mmol), ácido carboxibencenoborónico (3.98 g, 24.0 mmol), tetrakis(trifenilfosfina)- paladio(0) (0.74 g, 0.66 mmol), carbonato de potasio (9.7 g, 70 mmol), dimetilformamida (35 mL) y agua (17 mL) fueron cargados en una matraz de fondo redondo de tres cuellos equipada con un termómetro, un condensador de reflujo y agitación magnética. La mezcla fue purgada con nitrogeno y gradualmente calentada desde 81 a 95°C durante 9 horas. La cromatografía de capa delgada (acetato de etilo:hexano:ácido acético 4:6:0.5) mostró un rastro de material de inicio a Rf 90.7, producto a Rf 0.4 e impurezas a Rf 0.5 y 0.3. La mezcla fue enfriada a temperatura ambiente y dejada reposar durante 48 horas. Los sólidos fueron recolectados al vacío mediante filtración, lavados con 30 mL de etanol:agua 1:1 y guardados. El filtrado fue diluido con 210 mL de agua y 8 mL de solución de hidroxido de potasio 9N (a pH 12- 13), enfriado en un baño de hielo y agitado durante 30 minutos. Los sólidos fueron recolectados mediante filtración al vacío y lavados con 5 mL de agua para proporcionar 1 g de una mezcla de producto y un *spot running* con el material de inicio. Esta mezcla fue descartada. El filtrado fue enfriado en una baño de hielo y acidificado a pH 5- 6 con aproximadamente 10 mL de ácido acético. Los sólidos fueron recolectados mediante filtración al vácio, lavados con 10 mL de etanol:agua 1:1 secados al vacio para proporcionar 2.9 g (rendimiento de 37%) del ácido 4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]benzóico como un sólido de color marrón.

Ejemplos I- 172 a I- 181: Los compuestos de los ejemplos I- 172 a I- 181 fueron preparados según el procedimiento 4 a partir de del ácido 4- [6- amino- 5- (2- dicloro-benciloxi)- piridin- 3- il]- benzóico y: (2R)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo I- 172); (2S)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo I- 173); (3S)- 3- dimetilamino- pirrolidina (ejemplo I- 174); éster tert- butílico del ácido (S)- pirrolidin- 3- il- carbámico, seguido por desprotección del grupo Boc con ácido trifluoroacético en diclorometano (Ejemplo I- 175); 4- pirrolidin- 1- il- piperidina (Ejemplo I- 176); N- metilpiperazina (Ejemplo I- 177); 1- piperazin- 1- il- etanona (ejemplo I- 178); 1- metil- piperidin- 4- ilamina (Ejemplo I- 179); 2- morfolin- 4- il- etilamina (Ejemplo I- 180); y 3- morfolin- 4- il- propilamina (ejemplo I- 181).

Ejemplo I- 182: 5- Bromo- 3- (2- trifluorometil- benciloxi)- piridin- 2- ilamina (5.80 g, 16.7 mmol), ácido 4- carboxibencenoborónico (3.05 g, 18.4 mmol), tetrakis(trifenilfosfina)- paladio(0) (0.62 g, 0.6 mmol), carbonato de potasio (8.10 g, 58 mmol), dimetilformamida (47 mL) y agua (23 mL) fueron cargados en una matraz de fondo redondo de tres cuellos equipada con un termómetro, un condensador de reflujo y agitación magnetica. La mezcla fue purgada con nitrogeno y gradualmente calentada desde 81 a 93°C durante un periodo de 4 horas. La cromatografía de capa delgada (acetato de etilo:hexano:ácido acético 4:6:0.5) mostro producto a Rf 0.6 y pocas impurezas pequeñas. La mezcla fue enfriada a 45°C. Los sólidos fueron recolectados mediante filtración al vacío, lavados con 10 mL de etanol:agua 1:1 y descartados. El filtrado fue diluido con 300 mL de agua y 4 mL de solución de hidroxido de potasio 9 N (a pH 12- 13), enfriado en un baño de hielo y agitado durante 30 minutos con 3 g de Celite y 3g de Norit. Los sólidos fueron recolectados mediante filtración al vacío a través de un cojin de Celite y lavados con 10 mL de agua. Los sólidos fueron descartados. El filtrado fue enfriado en un baño de hielo y acidificado a pH 7.3 con ácido acético utilizando un medidor de pH. Los sólidos fueron recolectados mediante filtración al vacío, lavados con 20 mL de etanol:agua 1:1 y secados al vacío para proporcionar 4.5 g (rendimiento de 69%) del ácido 4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- benzóico como un sólido de color marrón.

Ejemplos I- 183 a I- 192: Los compuestos de los ejemplos I- 183 a I- 192 fueron preparados según el procedimiento 4 a partir del ácido 4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- benzóico y: (2R)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo I- 183); (2S)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo I- 184); (3S)- 3- dimetilamino- pirrolidina (Ejemplo I- 185); éter tert- butílico del ácido pirrolidin—3- ilcarbámico, seguido por desprotección del grupo Boc con ácido trifluoroacético en diclorometano (Ejemplo I- 186); 4- pirrolidin- 1- il- piperidina (Ejemplo I- 187); N- metilpiperazina (Ejemplo I- 188); 1- piperazin- 1- il- etanona (Ejemplo I- 187); N- metilpiperzina (Ejemplo I- 188); 1- piperazin- 1- il- etanona (Ejemplo I- 189); 1- metil- piperidin- 4- ilamina (Ejemplo I- 190); 2- morfolin- 4- il- etilamina (Ejemplo I- 191); y 3- morfolin- 4- il- propilamina (Ejemplo I- 192).

Ejemplo I- 193: 2- (2- amino- 5- bromo- piridin- 3- iloximetil- benzonitrilo (9.0 g, 26.8 mmol), ácido 4- carboxibencenoborónico (4.9 g, 30.0 mmol), tetrakis(trifenilfosfina)- paladio(0) (1.1 g, 1.0 mmol), carbonato de potasio anhidro (13.1 g, 95 mmol), dimetilformamida (72 mL), y agua (36 mL) fueron cargados en una matraz de fondo redondo de tres cuellos equipada con un termómetro, un condensador de reflujo y agitación magnética. La mezcla fue cargada con nitrogeno y gradualmente calentada desde 81 a 96°C durante un periodo de 2 horas. La cromatografía de capa delgada (acetato de etilo:hexano:ácido acético 4:6:0.5) mostró un rastro de material de inicio a Rf 0.8, producto a Rf 0.5 y una impureza a Rf 0.4. La mezcla fue enfriada a 45°C y filtrada para retirar los sólidos. El filtrado fue diluido con 432 mL de agua y 8 mL de solución de hidroxido de potasio 9N (a pH 12- 13), enfriada en un baño de hielo y se agregó 4 g de Celite y 2g de Norit. Los sólidos fueron recolectados mediante filtración al vacío a través de 4 g de Celite, lavados con 30 mL de etanol:agua 1:1 y descartados. El filtrado fue enfriado en un baño de hielo y acidificado con ácido acético a pH 7.5 utilizando un medidor de pH. Los sólidos fueron recolectados mediante filtración al vacío, lavados con 20 mL de agua y secados al vacío para proporcionar 8.1 g (rendimiento del 80%) ácido 4- [6- amino- 5- (4- tert- butil- benciloxi)- piridin- 3- il]- benzoico como un sólido oscuro.

Ejemplos I- 194 a I- 201: Los compuestos de los ejemplos I- 194 a I- 201 se prepararon según el procedimiento 4 a partir del ácido 4- [6- amino- 5- (4- tert- butil- benciloxi)- piridin- 3- il]- benzóico y: (2R)- 2- pirrolidin- 1- ilmetil- pirrolidina

(Ejemplo I- 194); (2S)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo I- 195); (3S)- 3- dimetilamino- pirrolidina (Ejemplo I- 196); N- metilpiperazina (Ejemplo I- 197); 1- piperazin- 1- il- etanona (Ejemplo I- 196); 1- metil- piperidin- 4- ilamina (Ejemplo I- 199); 2- morfolin- 4- il- etilamina (Ejemplo I- 200); y 3- morfolin- 4- il- propilamina (Ejemplo I- 201).

Ejemplo I- 202: 5- bromo- 3- (2- cloro- 4- fluoro- benciloxi)- piridin- 2- ilamina (9.00 g, 27.0 mmol), ácido 4- carboxibencenoborónico (4.41 g, 27.0 mmol), tetrakis(trifenilfosfina)- paladio(0) (0.99 g, 0.9 mmol), carbonato de potasio (13.1 g, 95 mmol), dimetilformamida (72 mL), y agua (36 mL) fueron cargados en una matraz de fondo redonde de tres cuellos equipada con un termómetro, un condensador de reflujo y agitación magnética. La mezcla fue purgada con nitrogeno y gradualmente calentada desde 81 a 98°C durante un periodo de 4 horas. La cromatografía de capa delgada (acetato de etilo:hexano:ácido acético 4:6:0.5) mostró un rastro de material de inicio a Rf 0.7, producto a Rf 0.4 y pocas impurezas. La mezcla fue enfriada a 45°C. Los sólidos fueron recolectados mediante filtración al vacío, lavados con 20 mL de etanol:agua 1:1 y descartados. El filtrado fue diluido con 432 mL de agua y 8 mL de solución de hidroxido de potasio 9N (a pH 12- 13), enfriados en un baño de hielo y agitados durante 30 minutos. Los sólidos fueron recolectados mediante filtración al vacío y lavados con 5 mL de agua para proporcionar aproximadamente 1 g de una mezcla que fue descartada. El filtrado fue enfriado en un baño de hielo y acidificado a pH 6.5 con ácido acético utilizando un medidor de pH. Los sólidos fueron recolectados mediante filtración al vacío, lavados con 10 mL de etanol:agua 1:1 y secados al vacío para proporcionar 3.6 g (36% de rendimiento) de ácido 4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- benzóico como un sólido de color marrón.

Ejemplos I- 203 a I- 210: Los compuestos de los ejemplos I- 203 a I- 210 fueron preparados según el procedimiento 4 a partir de 4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- benzóico y: (2R)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo I- 203); (2S)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo I- 204); (3S)- 3- dimetilamino- pirrolidina (Ejemplo I- 205); éster tert- butílico del ácido (S)- pirrolidin- 3- il- carbámico, seguido por la desprotección del grupo Boc con ácido trifluoroacético en diclorometano (Ejemplo I- 206); N- metilpiperazina (Ejemplo I- 207); 1- piperazin-

1- il)- etanona (Ejemplo I- 208); 2- morfolin- 4- il- etilamina (Ejemplo I- 209); y 3- morfolin- 4il- propilamina (Ejemplo I- 210).

Ejemplo I- 211: Se preparó éster metílico del ácido 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzóico siguiendo el procedimiento 3 a partir de 5- bromo- 3- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 2- ilamina y ácido 4- metoxicarbonilbencenoborónico como un solido blancuzco en rendimiento del 55%. 1H NMR (CDCl3, 300 Mhz), δ3.94 (s, 3H), 4.79 (brs, 2H), 5.29- 5.30 (d, 2H), J, 1.6), 7.06- 7.19 8dt, 1H, J, 4.1, 9.0), 7.2- 7.26 (m, 1H), 7.37- 7.38 (d, 1H, 1.8), 7.58- 7.61 (m, 2H), 8.01- 8.02 (d, 2H, J, 1.8), 8.08- 8.11 (m, 2H).

A una solución agitada de éster metílico del ácido 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzóico (2.5 g, 31 mol). La reacción se tornó de color naranja de manera inmediata y se dejo agitar a temperatura ambiente durante 18 horas. La reacción fue diluida con EtOAc (200 mL) y salmuera (50 mL). La capa orgánica fue separada y la capa acuosa fue extraída con EtOAc (2 x 50 mL). Las capas organicas fueron combinadas y lavadas con salmuera (2 x 25 mL), secadas con Na2SO4 y concentradas hasta sequedad al vacío para proporcionar ácido 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzóico (2.4 g, 6 mmol), 99%) como un sólido blancuzco.

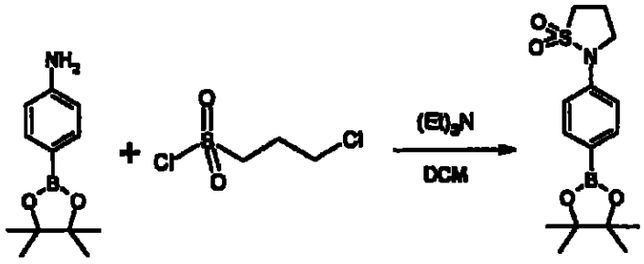
Ejemplos I- 212 a I- 224: Los compuestos de los ejemplos I- 212 a I- 224 fueron preparados según el procedimiento 4 a partir de ácido 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzóico y: N- metilpiperazina (ejemplo I- 212); 4- pirrolidin- 1- il- piperidina (Ejemplo I- 213); éster tert- butílico del ácido piperidin- 4- il- carbámico, seguido por desprotección del grupo Boc con ácido trifluoroacético en diclorometano (Ejemplo I- 214); 3,5- dimetil- piperazina (Ejemplo I- 215); (2S)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo I- 216); (3S)- 3- dimetilamino- pirrolidina (Ejemplo I- 217); éster tert- butílico del ácido (R)- pirrolidon- 3- il- carbámico, seguido por desprotección del grupo Boc con ácido trifluoroacético en diclorometano (Ejemplo I- 218); éster tert- butílico del ácido (S)- pirroldin- 3- il- carbámico, seguido por desprotección del grupo Boc con ácido trifluoroacético en diclorometano (Ejemplo I- 219); 1- metil- piperidin- 4- ilamina (Ejemplo I- 220); 2- pirrolidin- 1- il- etilamina

(Ejemplo I- 221); 3- pirrolidin- 1- il- propilamina (Ejemplo I- 222); 2- morfolin- 4- etilamina (Ejemplo I- 223); y 3- morfolin- 4- il- propilamina (Ejemplo I- 224).

Ejemplo I- 225: Se preparó ácido 3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzóico utilizando el mismo procedimiento que para el ácido 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzóico a partir de 5- bromo- 3- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 2- ilamina y ácido 3- metoxicarbonilbencenoborónico.

Ejemplos de I- 226 a I- 239: Los compuestos de los ejemplos I- 226 a I- 239 se prepararon según el procedimiento 4 a partir de ácido 3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzóico y: N- metilpiperazina (Ejemplo I- 226); 4- pirrolidin- 1- il- piperidina (Ejemplo I- 227); éster tert- butílico del ácido piperidin- 4- il- carbámico, y luego seguido por la desprotección del grupo Boc con ácido trifluoroacetico en diclorometano (Ejemplo I- 228); 3,5- dimetil- piperazina (Ejemplo I- 229); (2S)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo I- 230); (3S)- 3- dimetilamino- pirrolidina (Ejemplo I- 231); éster tert- butílico del ácido (R)- pirrolidin- 3- il- carbámico, seguido por desprotección del grupo Boc con ácido trifluoroacético en diclorometano (Ejemplo I- 232); éster tert- butílico del ácido (S)- pirrolidin- 3- il- carbámico, seguido por desprotección del grupo Boc con ácido trifluoroacético en diclorometano (Ejemplo I- 233); 1- metil- piperidin- 4- ilamina (Ejemplo I- 234); 2- pirrolidin- 1- il- etilamina (Ejemplo I- 235); 3- pirrolidin- 1- il- propilamina (Ejemplo I- 236); 2- morfolin- 4- il- etilamina (Ejemplo I- 237); 3- morfolin- 4- il- propilamina (Ejemplo I- 238); y 1- [4- (2- amino- etil)- piperzin- 1- il]- etanona (Ejemplo I- 239).

Ejemplo I- 240:



1. Se disolvió 4- (4,4,5,5- Tetrametil- 1,3,2- dioxaborolan- 2- il)anilina (5g, 22.8 mmol) en DCM (100 mL, 0.1M), se agregó a la mezcla trietilamina (15 mL, 5.0 molar

equivalente). La reacción fue agitada a 0°C durante 5 min, se agregó cloruro de 3-cloropropano- 1- sulfonilo (4.2 g, 23.0 mmol). La reacción fue agitada a 0°C durante 1 hora y llevada gradualmente a temperatura ambiente, calentada a reflujo a 70°C duante 2 horas. La mezcla fue enfriada a temperatura ambiente, diluida con EtOAc y agua. La capa organica fue lavada con salmuera, secada sobre MGSO4, filtrada y concentrada. El residuo fue purificado a través de columna de sílice para proporcionar 2- [4- (4,4,5,5-tetrametil- 1,3,2- dioxaborolan- 2- il)fenil]isotiazolidina 1,1- dioxido como un sólido blancuzco (5.2 g, rendimiento del 70%). 1H NMR (400 MHz, DMSO- d6) δ 7.62 (d, 2H), 7.18 (d, 2H), 3.76 (t, 2H), 3.53 (t, 2H), 2.41 (t, 2H), 1.28 (s, 12H).

2. Se preparó 3- (2- Cloro- 3,6- difluoro- benciloxi)- 5- [4- (1,1- dioxo- 1Å- isotiazolidin- 2- il)- fenil]- piridin- 2- ilamina siguiendo el procedimiento 3 a partir de 1,1- dioxido de 5- bromo- 3- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 2- ilamina y 2- [4- (4,4,5,5- tetrametil- 1,3,2- dioxaborolan- 2- il)fenil]isotiazolidina.

Ejemplo I- 241: Se preparó 3- (2,6- difluoro- benciloxi)- 5- [4- (1;1- dioxo- 1λ^6- isotiazolin- 2- il)- fenil]- piridin- 2- ilamna siguiendo el procedimeinto 3 a partir de 5- bromo- (2,6- difluoro- benciloxi)- piridin- 2- ilamina y 2- [4- (4,4,5,5- tetrametil- 1,3,2- dioxaborolan- 2- il)- fenil]iso- tiazolidina- 1,1- dioxido.

Ejemplo I- 242: Se preparó 5- [4- (1;1- dioxo- 1λ^6- isotiazolin- 2- il)- fenil]- 3- (2- fluoro- 6- trifluorometil- benciloxi)- piridin- 2- ilamna según el procedimiento 8.

Ejemplo I- 243: Se sintetizó {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- dietilamino- etanosulfónico según el procedimiento 9.

Ejemplos I- 267 a I- 269: Los compuestos de los ejemplos I- 267 a I- 269 fueron preparados según el procedimiento 3, con purificación por HCLP preparativa de fase inversa eluyendo con sistema acetonitrilo- agua- ácido trifluoroacetico y se obtuvieron como sales de ácido, a partir de 5- bromo- 3- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 2- ilamina y: ácido 2- (dimetilaminometil)- fenilboronico (Ejemplo I- 267);

ácido 3- (pirrolidin- 1- il)- fenilboronico (Ejemplo I- 268) y N- [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)fenil]- metanosulfonamida (Ejemplo I- 269).

Ejemplo I- 270: Se preparó ácido5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3-]- tiofeno- 2- carboxilico siguiendo el procedimiento 3 comenzando a partir del ácido 5- bromo- 3- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 2- ilamina y carboxitiofeno- 2- boronico.

Ejemplos I- 271 a I- 276: Los compuestos de los ejemplos I- 271 a I- 276 fueron preparados según el procedimiento 4 a partir de 5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofeno- 2- carboxilico y; N- metilpiperazina (ejemplo I- 271); (2R)- 2- pirrolidin- 1- ilmetil- pirrolidina(Ejemplo I- 272); 1- metil- piperidin- 4- il)- amina (Ejemplo I- 273); 3,5- dimetil- piperazina (Ejemplo I- 274); 2- pirrolidin- 1- il- etilamina (Ejemgplo I- 275); y 4- pirrolidin- 1- il- piperidina (Ejemplo I- 276).

Ejemplo I- 277: Se preparó ácido 4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3-]- benzoico según el mismo procedimiento como ácido 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzoico a partir de ácido 5- bromo- 3- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 2- ilamina y 4- metoxicarbonilbencenoboronico.

Ejemplos I- 278 a I- 285: Ejemplos I- 278 a I- 285 fueron preparados según el procedimiento 4 a partir de ácido 4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- benzoico y 4- pirrolidin- 1- il- piperidina (Ejemplo I- 278); 1- metil- 4- ilamina (Ejemplo I- 279); 3,5- dimetil- piperazina (Ejemplo I- 280); 3- dimetilamino- pirrolina (Ejemplo I- 281); (2S)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo I- 282); 2- morfolin- 4- il- etilamina (Ejemplo I- 283); N- metilpiperazina (Ejemplo I- 284); y 4- acetil- piperazin- 1- il)- etilamina (Ejemplo I- 285).

Ejemplos I- 286- 289: los compuestos de los ejemplos I- 286 a I- 289 fueron preparados siguiendo el procedimiento 9.

Ejemplo I- 290: Se preparó ácido 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- benzoico utlizando el mismo procedimiento como ácido

4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzoico a partir de ácido 5- bromo- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]piridin- 2- ilamina y 4- metoxicarbonilbencenoboronico.

Ejemplos I- 291 a I- 296: los compuesto de los ejemplos I- 291 a I- 296 fueron preparados según el procedimiento 4 a partir de ácido 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- benzoico y (2R)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo I- 291); 1- metil- piperidin- 4- ilamina (Ejemplo I- 292); éster tert- butilo del ácido (R)- pirrolidin- 3- il- carbamico, seguido por desprotección del grupo Boc con ácido trifluoroacetico en diclorometano (Ejemplo I- 293); 4- pirrolidin- 1- il- piperidina (Ejmeplo I- 294); N- metil- piperazina (Ejemplo I- 295) y 3,5- dimetil- piperazina (Ejemplo I- 296).

Ejemplos I- 297 a I- 299: los compuestos de los ejemplos I- 297 a I- 299 fueron preparados siguiendo el procedimiento 9.

Ejemplos I- 300 a I- 661 los ejemplos fueron preparados según los procedimientos citados en las tablas en la presente, excepto como se describió en los siguientes párrafos. Cuando múltiples procedimientos son citados en las tablas separados por "/", los procedimientos indicados fueron realizados secuencialmente

Ejemplo I- 311: Se preparó ácido 3- {6- amino- 5- [1- 82,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- benzoico utilizando el mismo procedimiento como ácido 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi9- piridin- 3- il]- benzoico a partir de 5- bromo- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina y ácido metoxicarbonilbencenoboronico.

Ejemplo I- 312: Se preparó 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona siguiendo el procedimiento a partir de 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- benzoico y 1- metil- piperidin- 4- ilamina.

Ejemplo I- 330: Se preparó ácido 4- {6- amino- 5- [1- (2- cloro- 3- difluoro- fenil)- etoxi]- piridin- 3- il}- benzoico utilizando el mismo procedimiento como ácido

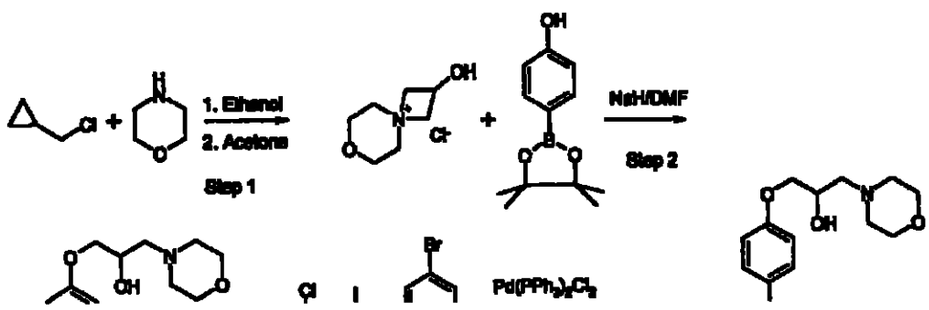
4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzoico a partir de ácido 5- bromo- 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 2- ilamina y ácido 4- metoxicarbonilbencenoboronico.

Ejemplo I- 331: Se preparó 4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida siguiendo el procedimiento 4 comenzando a partir del ácido 4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il]- benzoico y la correspondiente amina.

Ejemplo I- 342: Se preparó ácido 4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- benzoico. Utilizando el mismo procedimiento como ácido 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzoico a partir de 5- bromo- 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 2- ilamina y ácido 3- metoxicarbonilbencenoboronico.

Ejemplo I- 343: Se preparó (3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona siguiendo el procedimiento 4 comenzando a partir del ácido 3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- benzoico y la correspondiente amina.

Ejemplo I- 359: preparación de 2- hidroxi- 7- oxa- 4- azonia- spiro[3,5]nonano: a una solución de morofolina (17.4 mL; 0.2 mol,1.0 eq)en etanol (20 mL)se Agregó epiclorohidrin (16.1 ml, 1.03 eq)desde el embudo de adición. La reacción fue enfriada con un baño de agua helada y gradualmente se elevo a temperatura ambiente. Después de 24 horas, la reacción fue concentrada a 50°C hasta que no se condensar mas destilado. El aceite resultante fue almacenada a temperatura ambiente hasta que se observó una masa significativa de cristales. La lechada fue diluida con acetona y filtrada. Los sólidos fueron bajo alto vacío. Esto proporciono 20 g de producto cristalino. Las aguas madres pudieron ser concentradas y el proceso de cristalización repetido en recuperación de aumento.



330.

2.Preparación de 1- morfolin- 4- il- 3- [4,4,5,5- tetrametil- [1,3,2]dioxoborolan- 2- il)- fenoxi]- propan- 2- ol:4- (4,4,5,5- tetrametil- [1,3,2]dioxoborolan- 2- il)- fenol (440 mg,2 mmol)se agregó a una suspención agitada deNaH (96mg, 2eq)en diclorometano a 0°C. Después de 1 hora se agregó 2- hidroxi- 7- oxa- 4- azonia- spiro[3.5]nonano (714mg, 2eq). La mezcla fue agitada a temperatura ambiente durante la noche. La mezcla de reacción fue vertida en una solución de NH4Cl saturado, y extraída con acetato de etilo. Los extractos fueron lavados con salmuera secados sobre Na2SO4 y condensados a sequedad. El producto crudo fue purificado con una columna de gel de sílice eluyendo con metanol al 2% en cloruro de metileno para proporcionar 220 mg de producto como un sólido rosado (30%). ^{1}H NMR (400 MHz, DMSO- d6): δ 7.58 (d, J=8.2 Hz, 2H), 6.915 8d, J=7.8 Hz, 2H), 4.89 (d, J=2.0Hz, 1H), 3.98 (m, 3H), 3.55 (m, 4H), 2.40 (m, 6H), 1.27 (s, 12H). MS (m/e): 364 $[m+H]^+$ (100%).

3. Se preparó (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenoxi)- 3- morfolin- 4- il- propan- 2- ol siguiendo el procedimiento 3 comenzando a partir de 5- bromo- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina y 1- morfolin- 4- il- 3- [4,4,5,5- tetrametil- [1,3,2]dioxoborolan- 2- il)- fenoxi]- propan- 2- ol:

Ejemplo I- 371: Se preparó (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil- amida según el procedimiento 10.

Ejemplo I- 386: Se preparó ácido 3- {amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- benzoico utilizando el mismo procedimiento como ácido 4[6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzoico a partir de 5- bromo- 3- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 2- ilamina y ácido 3- metoxicarbonilbencenoboronico.

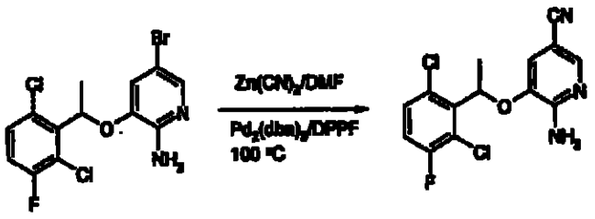
331

Ejemplo I- 387: Se preparó ácido 3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il) metanona siguiendo el procedimiento 4 comezando a partir de ácido 3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]piridin- 3- il}- benzoico y 3,5- dimetil- piperazina.

Ejemplo 399: Se preparó ácido 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- benzoico utilizando el mismo procedimiento comenzando como ácido 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzoico a partir de 5- bromo- 3- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 2- ilamina y ácido 4- metoxicarbonilbencenoboronico.

Ejemplo 400: Se preparó 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida siguiendo el procedimiento 4 comenzando a partir de ácido 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- benzoico y 2- pirrolidin- 1- il- etilamina.

Ejemplo I- 454:



A una solución de 5- bromo- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina (5.00 g,13.1 mmol) en DMF (73 mL) y agua (1 mL)se agregó Zn(CN)2 (4.50 g,26.3 mmol), Pd2(dba)3 (0.602 g,0.65 mmol), y DPPF (0.86 g, 1.55 mmol). La mezcla fue degasificada y cargada con nitrógeno durante tres veces, luego agitada bajo nitrógeno a 100°C durante 3 horas. La solución de reacción fue particionada entre acetato de etilo y agua. La capa orgánica fue lavada con una solución de NH4Cl- concentrada saturada, NH4OH- agua (4:1:4), luego secada sobre MgSo4. El producto crudo fue purificado sobre una columna de gel de sílice eluyendo con acetato

de etilo- hexanos (1:4) para proporcionar 6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- nicotinonitrilo como un solido blanco (4.15 g, rendimiento 97%).

Ejemplo I- 455: Se obtuvo 6- amino- 5- [1- (2,6- dicloro- 3- ciano- fenil)- etoxi]- nicotinonitrilo como un producto secundario a partir de la preparación de 6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- nicotinonitrilo.

Ejemplol- 456: Se preparó 5- aminometil- 3- [- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina con la reducción de 6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- nicotinonitrilo. A una solución de borano en THF(1.0 M, 16.8 mL) se agregó 6- amino- 5[1- 82,6- dicloro- 3- fluoro- fenil)- etoxi]- nicotinonitrilo (785 mg, 2.41 mmol) en THF anhidro (8 mL)a 0°C bajo nitrógeno. La solución de reacción fue agitada bajo nitrógeno a 0°C durante 5 horas, luego se agregó la solución de HCl (6N, 12 mL)lentamente siguiendo con la adición de agua (12 mL) y metanol (80 mL). La mezcla fue agitada durante la noche. Después de evaporación de solventes, el residuo fue particionado entre diclorometano y solución de NaOH (1N). La capa de agua fue extraída tres veces y los extractos combinados fueron secados sobre MgSO4. Después de filtración, evaporación y secado a alto vacío, se obtuvo un producto sólido blanco (750 mg, rendimiento 94%).

Ejemplo I- 457: Se preparó {6- amino- 5- [1- (2,6- dicloro- 3- fluro- fenil)- etoxi]- piridin- 3- ilmetil}- amida del ácido (R)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxilico con el mismo procedimiento como el paso 4 en el procedimiento 11.

Ejemplo I- 462: Se preparó (S)- 1- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- etano- 1,2- diol como sigue: a una solución de mezcla de dihidroxilación asimétrica α (2.33 g) en una mezcla 1:1 de T- BuOH y agua (8 mL cada uno) enfriada a 0°C se agregó 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- vinil- piridin- 2- ilamina (500 mg, 1.67 mmol). La mezcla de reacción fue agitada a 0°C hasta consumir el material de inicio. Se agregaron tres cargas más de mezcla AD α periódicamente para aumentar la tasa de reacción. Se agregó agua (5 mL) y la mezcla fue extraída con EtOAc(3 x 20 mL). La capa orgánica combinada fue secada sobre Na2SO4 y concentrada. El producto crudo fue purificado mediante HPLC de fase

inversa para proporcionar (S)- 1- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- etano- 1,2- diol (320 mg, rendimiento 53%).

Ejemplo I- 463: Se preparó(R)- 1- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- etano- 1,2- diol con el mismo procedimiento como en el ejmplo I- 462 con AD- mix α.

Ejemplos II- 1 a II- 6: Los compuestos de los ejemplos II- 2 a II- 6 fueron preparados según el procedimiento 3 para acoplamiento Suzuki a partir de 5- bromo- 3- (2,6- dicloro- benciloxi)- pirazin- 2- ilamina y: 4- (4,4,5,5- tetrametil- [1- 3,2]dioxaborolan- 2- il)- fenol (Ejemplo II- 1); 2- [4- (4,4,5,5- tetrametil- 1- 3,2- dioxaborolan- 2- il)- fenil]isotiazolidina- 1,1- dioxido (Ejemplo II- 2); 3- {2- [4- (4,4,5,5- tetrametil- [1- 3,2]dioxaborolan- 2- il)- etil}- morfina (Ejemplo II- 3); 4- {2- [4- (4,4,5,5- tetrametil- [1- 3,2]dioxaborolan- 2- il)- fenoxi]- etil}- morfina (Ejemplo II- 4); 4- (4,4,5,5- tetrametil- [1- 3,2]dioxaborolan- 2- il)- fenilamina (Ejemplo II- 5); ácido 4- (4,4,5,5- tetrametil- [1- 3,2]dioxaborolan- 2- il)- benzoico (Ejemplo II- 6).

Ejemplo II- 7: Se preparó {4- [5- amino- 6- (2,6- dicloro- benciloxi)- pirazin- 2- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona siguiendo el procedimiento de amidación 4 a partir del ácido {4- [5- amino- 6- (2,6- dicloro- benciloxi)- pirazin- 2- il]- benzoico y(2R)- 2- pirrolidin- 1- ilmetil- pirrolidina.

Ejemplo II- 8: se preparó {4- [5- amino- 6- (2,6- dicloro- benciloxi)- pirazin- 2- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona siguiendo el procedimiento de amidación 4 a partir del ácido 4- [5- amino- 6- (2,6- dicloro- benciloxi)- pirazin- 2- il]- benzoico y 4- pirrolidin- 1- il- piperidina.

Ejemplos II- 9 a II- 32: Los compuestos de los ejemplos II- 9 a II- 32 fueron preparados siguiendo el procedimiento de el procedimiento de acoplamiento Suzuki 3 a partir de 5- bromo—3- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- ilamina y siguiendo los compuestos preparados según el procedimiento en el ejemplo I- 243: [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- morfolin- 4- il- etanosulfónico (Ejemplo II- 9); [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- piperidin- 1- il- etanosulfónico (Ejemplo II- 10); [4- (4,4,5,5-

tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico (Ejemplo II- 11); [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- pirrolidin- 1- il- etanosulfónico (Ejemplo II- 12); [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- [(3R)- 3- hidroxi- pirrolidin- 1- il]- etanosulfónico (Ejemplo II- 13);++ [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido [(2S)- 2- hidroximetil- pirrolidin- 1- il]- etanosulfónico (Ejemplo II- 14); [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- (ciclopropilmetil- amino)- etanosulfónico (Ejemplo II- 15); [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- dimetilamino- etanosulfónico (Ejemplo II- 16); [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- dietilamino- etanosulfónico (Ejemplo II- 17); [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- (4- acetil- piperazin- 1- il)- etanosulfónico (Ejemplo II- 18); [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- [4—(2- hidroxi- acetil)- piperazin- 1- il]- etanosulfónico (Ejemplo II- 19); [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- ciclopropilamino- etanosulfónico (Ejemplo II- 20); [3- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2[(3R)- 2- hidroximetil- pirrolidin- 1- il]- etanosulfónico (Ejemplo II- 21); [3- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico (Ejemplo II- 22); [3- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- (4- acetil- piperazin- 1- il)- etanosulfónico (Ejemplo II- 23); [3- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- piperidin- 1- il- etanosulfónico (Ejemplo II- 24);+++ [3- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- dietilamino- etanosulfónico (Ejemplo II- 25); [3- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- morfolin- 4- il- etanosulfónico (Ejemplo II- 26); [3- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- pirrolidin- 1- il- etanosulfónico (Ejemplo II- 27); [3- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- dimetilamino- etanosulfónico (Ejemplo II- 28); [3- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- [4- (2- hidroxi- acetil)- piperazin- 1- il]- etanosulfónico (Ejemplo II- 29); [3- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- (ciclopropilmetil- amino)- etanosulfónico (Ejemplo II- 30); [3- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- [(3R)- 3- hidroxi- pirrolidin- 1- il]- etanosulfónico (Ejemplo

II- 31); [3- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenil]- amida del ácido 2- ciclopropilamino- etanosulfónico (Ejemplo II- 32).

Ejemplo II- 33: Se preparó ácido 4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- benzoico siguiendo el procedimiento de acoplamiento Suzuki 3 a partir de 5- bromo- 3- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- ilamina y ácido 4- (4,4,5,5- tetrametil- [1,3,2]dioxa- borola- 2- il)- benzoico.

Ejemplo II- 34: Se preparó {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona siguiendo el procedimiento de amidacion 4 a partir de ácido 4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)pirazin- 2- il]- benzoico y (2R)- 2- pirrolidin- 1- ilmetil- pirrolidina.

Ejemplos II- 35 a II- 46: los compuestos de los ejemplos II- 35 a II- 46 según el procedimiento de amidación 4 a partir de 4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il- benzoico y: 2- pirrolidin- 1- il- etilamina (Ejemplo II- 35); éster tert- butilico del ácido (S)- pirrolidin- 3- il- carbamico, seguido por desprotección del grupo Boc con ácido trifluoroacetico en diclorometano (Ejemplo II- 36); 1- [4- (2- amino- etil)- piperazin- 1- il]- etanona (Ejemplo II- 37); 3- pirrolidin- 1- il- propilamina(Ejemplo II- 38); (3S)- 3- dietilamina- pirrolidina (Ejemplo II- 39); éster tert- butilico del ácido(R)- pirrolidin- 3- il- carbamico seguido por desprotección del grupo Boc con ácido trifluoroacetico en diclorometano (Ejemplo II- 40); 3,5- dimetil- piperazina (Ejemplo II- 41); 4- pirrolidin- 1- il- piperidina (Ejemplo II- 42); 3- morfolin- 4- ilpropilamina (Ejemplo II- 43); 1- metil- piperidin- 4- ilamina (Ejemplo II- 44); 2- morfolin- 4- il- etilamina (Ejemplo II- 45); y N- metilpiperazina (Ejemplo II- 46).g

Ejemplo II- 47: se preparó 3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi9- pirazin- 2- il]- benzoico siguiendo el procedimiento de acoplamiento Suzuki del procedimiento 3 a partir de 5- bromo- 3- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- ilamina (Ejemplo II- (b));y ácido 3- (4,4,5,5- tetrametil- [1,3,2]ddioxaborolan- 2- il)- benzoico (Aldrich, Milwaukee).

Ejemplos II- 48 a II- 60: los compuestos de los ejemplos II- 48 a II- 60 fueron preparados según el procedimiento de amidación 4 a partir de ácido 3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- benzoico Y: N- metilpiperazina (Ejemplo II- 48); éster tert- butilico del ácido (R)- pirrolidin- 3- il- carbamico, siguiendo por desprotección del grupo Boc con ácido trifluoroacetico en diclorometano (Ejemplo II- 49); éster tert- butilico del ácido (s)- pirrolidin- 3- il- carbamico siguiendo por desprotección del grupo Boc con ácido trifluoroacetico en diclorometano (Ejemplo II- 50);3,5- dimetil- piperazina (Ejemplo II- 51); 3- morfolin- 4- il- propilamina (Ejemplo II- 52); 4- pirrolidin- 1- il- piperidina (Ejemplo II- 53);(3S)- 3- dimetilamino- pirrolidina(Ejemplo II- 54);2- pirrolidin- 1- il- etil- amina (Ejemplo II- 55);1- metil- piperidin- 4- ilamina (Ejemplo II- 56); ((2S)- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo II- 57);2- morfolin- 4- il- etilamina (Ejemplo II- 58);2- (4- acetil- piperazin- 1- il)- etilamina (Ejemplo II- 59); y 3- pirrolidin- 1- il- propilamina (Ejemplo II- 60).

Ejemplo II- 61: Se preparó 3- (2- cloro- 3,6- difluro- benciloxi)- 5- (1H- indol- 5- il)- piperazin- 2- ilamina a partir de 5- bromo- 3- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- ilamina) y ácido indol- 5- boromico siguiendo el procedimiento 3.

Ejemplos II- 62 a II- 68: los compuestos de los ejemplos II- 62 a II- 68 preparados según el procedimiento 5 a partir de 3- (2- cloro- 3,6- difluro- benciloxi)- 5- (1H- indol- 5- il)- pirazin- 2- ilamina y: pirrolidina (Ejemplo II- 62); dietilamina (Ejemplo II- 63); 1- piperazin- 1- il- etanona (Ejemplo II- 64); 2,6- dimetil- morfolina (Ejemplo II- 65); N- (S)- pirrolidin- 3- il- acetamida (Ejemplo II- 66); piperidina (Ejemplo II- 67); y morfolina (Ejemplo II- 68).

Ejemplo II- 69: Se preparó 3- [1- (2- cloro- 3,6- difluro- fenil)- 2- metil- propoxi]- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- pirazin- 2- ilamina siguiendo el procedimiento de acoplamiento Suzuki 3 a partir de 5- bromo- 3- [1- (2- cloro- 3,6- difluro- fenil)- 2- metil- propoxi]- pirazin- 2- ilamina y 4- {2- [4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenoxi]- etil}- morfina

Ejemplo II- 70: Se preparo (3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- pirazin- 2- ilamina, compuesto con ácido trifluoroacetico siguiendo el procedimiento de acoplamiento Suzuki 3 a partir de 5-

bromo- 3- [1- (2- cloro- 3,6- difluoro- fenil)- 2- metil- propoxi]- pirazin- 2- ilamina y 4- {2- [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenoxi]- etil}- morfina. El producto fue purificado con HPLC preparativa de fase inversa C- 18 eluyendo con acetonitrilo- agua- ácido trifluroacetico y obtenido como una sal del ácido trifluoroacetico.

Ejemplos II- 71 a II- 83: Los compuestos de los ejemplos II- 71 a II- 83 fueron preparados según el procedimiento de acoplamiento Suzuki 3 a partir de 5- bromo- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- ilamina y: 4- {2- [4- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- fenoxi]- etil- morfina, seguido por purificación con HPLC preparativa de fase inversa C- 18 eluyendo con acetonitrilo- agua- ácido trifluroacetico y obtenido como una sal del ácido trifluoroacetico (Ejemplo II- 71); N- [4- (4,4,5,5- tetrametil- [1,3, 2]dioxaborolan- 2- il)- fenil]metano- sulfonamida (Ejemplo II- 72); [4- (4,4,5,5,- tetrametil[1,3,2]dioxoborolan- 2- il)- fenil]- amida del ácido 2- pirrolidin- 1- il- etanosulfónico (preparada como en el ejemplo I- 243)(ejemplo II- 73); [4- (4,4,5,5,- tetrametil[1,3,2]dioxoborolan- 2- il)- fenil]- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico (preparada como en el ejemplo I- 243)(ejemplo II- 74); [4- (4,4,5,5,- tetrametil[1,3,2]dioxoborolan- 2- il)- fenil]- amida del ácido 2- piperidin- 1- il- etanosulfónico (preparada según el procedimiento en el ejemplo I- 243)(ejemplo II- 75); [4- (4,4,5,5,- tetrametil[1,3,2]dioxoborolan- 2- il)- fenil]- amida del ácido 2- (ciclopropilmetil- amino)- etanosulfónico (preparada como en el ejemplo I- 243)(ejemplo II- 76); [4- (4,4,5,5,- tetrametil[1,3,2]dioxoborolan- 2- il)- fenil]- amida del ácido 2- [(3R)- 3- hidroxi- pirrolidin- 1- il]- etanosulfónico (preparada como en el ejemplo I- 243)(ejemplo II- 77); [4- (4,4,5,5,- tetrametil[1,3,2]dioxoborolan- 2- il)- fenil]- amida del ácido 2- [(2S)- 2- hidroximetil- pirrolidin- 1- il]- etanosulfónico (preparada como en el ejemplo I- 243)(ejemplo II- 78); [4- (4,4,5,5,- tetrametil[1,3,2]dioxoborolan- 2- il)- fenil]- amida del ácido 2- dimetilamino- etanosulfónico (preparada como en el ejemplo I- 243)(ejemplo II- 79); [4- (4,4,5,5,- tetrametil[1,3,2]dioxoborolan- 2- il)- fenil]- amida del ácido 2- morfolin- 4- il- etanosulfónico (preparada como en el ejemplo I- 243)(ejemplo II- 80); [4- (4,4,5,5,- tetrametil[1,3,2]dioxoborolan- 2- il)- fenil]- amida del ácido 2- dietilamino- etanosulfónico (preparada como en el ejemplo I- 243)(ejemplo II- 81); [4- (4,4,5,5,- tetrametil[1,3,2]dioxoborolan- 2- il)- fenil]- amida del ácido 2- ciclopropilamino-

etanosulfónico (preparada como en el ejemplo I- 243)(ejemplo II- 82); y ácido 3-(4,4,5,5,- tetrametil[1,3,2]dioxoborolan- 2- il)- benzoico (ejemplo II- 83);

Ejemplos II- 84 a II- 88: los compuestos de los ejemplos II- 84 a II- 88 fueron preparados según el procedimiento de la amidación 4 a partir de ácido 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)etoxi]pirazin- 2- il}- benzoico Y éster tert- butilico del ácido(S)- pirrolidin- 3- il- carbamico, seguido por desprotección del grupo Boc con ácido trifluroacetico en diclorometano (EjemploII- 84); éster tert- butilico del ácido(R)- pirrolidin- 3- il- carbamico, seguido por desprotección del grupo Boc con ácido trifluroacetico en diclorometano (EjemploII- 85); (2R)- 2- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo II- 86); 2- (4- acetil- piperazin- 1- il)- etilamina (Ejemplo II- 87); y (2S)- pirrolidin- 1- ilmetil- pirrolidina (Ejemplo II- 88).

Ejemplo II- 89: Se preparo ácido 3- {5- amino—6- [1- (2- cloro- 3,6- difluro- fenil)- etoxi]pirazin- 2- il}- benzoico siguiendo el procedimiento de acoplamiento Suzuki 3 a partir de 5- bromo- 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]pirazin- 2- ilamina y ácido3- (4,4,5,5- tetrametil[1,3,2]dioxaborolan- 2- il)- benzoico.

Ejemplo II- 90: Se preparó 3- {5- amino—6- [1- (2,6- dicloro- 3- fluro- fenil)- etoxi]pirazin- 2- il}- N- (1- metil- piridin- 4- il)benzamida siguiendo el procedimiento de amidación 4 a partir de ácido 3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]pirazin- 2- il}- benzoico y 1- metil- piperidin- 4- ilamina.

Ejemplo II- 91: Se preparo 3- {5- amino—6- [1- (2,6- dicloro- 3- fluro- fenil)- etoxi]pirazin- 2- il}- N- (3- pirrolidin- 1- il- propil)- benzamida siguiendo el procedimiento de amidación 4 a partir de ácido 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]pirazin- 2- il}- benzoico y 3- pirrolidin- 1- il- propilamina.

Ejemplo II- 92: Se preparo 3- {5- amino—6- [1- (2,6- dicloro- 3- fluro- fenil)- etoxi]pirazin- 2- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona siguiendo el procedimiento de amidación 4 a partir de ácido 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- benzoico y 4- pirrolidin- 1- il- piperidin –1- ilamina.

Ejemplo II- 93: Se preparo ácido 4- {5- amino—6- (3- fluro- 2- trifluorometil- benciloxi)- pirazin- 2- il}- benzoico siguiendo el procedimiento de acoplamiento Suzuki 3 a partir de 5- bromo- 3- [1- (3- fluoro- 2- trifluorometil- bencioxi)- pirazin- 2- ilamina y ácido 3- (4,4,5,5- tetrametil- [1,3,2]dioxaborolan- 2- il)- benzoico.

Ejemplo II- 94: Se preparo 4- [5- amino—6- [1- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- N- (2- morfolin- 4- il- etil)- benzamida siguiendo el procedimiento de amidación 4 a partir de ácido 4- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il}- benzoico y 2- morfolin- 4- il- etilamina.

Ejemplo II- 95: Se preparó 4- [5- amino- 6- (3- fluoro- 2- trifluorometil- bencilxoi)- pirazin- 2- il]- N- (1- metil- piperidin- 4- il)- benzamida siguiendo el procedimiento de amidación 4 a partir del ácido 4- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- benzóico y 1- metil- piperidin- 4- ilamina.

Ejemplos II- 96 a II- 211 se prepararon según el procedimiento citado en las Tablas en la presente, excepto como se describió específicamente en los siguientes párrafos.

Ejemplo II- 108: El ácido 4- (5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il]- benzóico se preparó utilizando el mismo procedimiento que para 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzóico a partir de 5- bromo- 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- ilamina y ácido 4- metoxicarbonilbencenoborónico.

Ejemplo II- 109: Se preparó 4- [5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il)- N- (3- pirrolidin- 1- il- propil)- benzamida siguiendo el

procedimiento 4 comenzando a partir del ácido 4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- benzóico y 3- pirrolidin- 1- il- propilamina.

Ejemplo II- 121: Se preparó ácido 3- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- benzóico utilizando los mismos procedimientos que para ácido 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]benzóico a partir de 5- bromo- 3- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- ilamina y ácido 3- metoxicarbonilbencenoborónico.

Ejemplo II- 122 Se preparó {3- [5- amino- 6- (3- fluoro- 2- trifluometil- benciloxi)- pirazin- 2- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona siguiendo el procedimiento 4 comenzando a partir del ácido 3- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- benzóico y 4- pirrolidin- 1- il- piperidin- 1- ilamina.

Ejemplo II- 145: Se preparó acido 4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- 3- fenil)- etoxi]- pirazin- 2- il}- benzóico utilizando el mismo procedimiento que para el ácido 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]benzóico a partir de 5- bromo- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- ilamina y ácido 4- metoxicarbonilbencenoborónico.

Ejemplo II- 148: Se preparó 4- [5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (R)- 2- hidroxi- 3- pirrolidin- 1- il- propil)- benzamida siguiendo el procedimiento 4 comenzando a partir del ácido 4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- 3- fenil)- etoxi]- pirazin- 2- il}- benzóico y (R)- 2- hidroxi- 3- pirrolidin- 1- il- propilamina.

Ejemplo II- 156: Se preparó ácido 4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- benzóico utilizando el mismo procedimiento que para ácido 4- [6- amino- 5- (2- cloro- 3,5- difluoro- benciloxi)- piridin- 3- il]- benzóico a partir de 5- bromo- 3- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- ilamina y ácido 4- metoxicarbonilbencenoborónico.

Ejemplo II- 157: Se preparó (4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona siguiendo el procedimiento 4 comenzando a partir de ácido 4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- benzóico y 4- pirrolidin- 1- il- piperidin- 1- ilamina.

Ejemplo II- 168: Se preparó Acido 3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- benzóico utilizando el mismo procedimiento que para el ácido 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzóico a partir de 5- bromo- 3- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- ilamina y ácido 3- metoxicarbonilbencenoborónico.

Ejemplo II- 169: Se preparó 3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il)- N- (1- metil- piperidin- 4- il)benzamida siguiendo el procedimiento 4 comenzando a partir de ácido 3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- benzóico y 1- metil- piperidin- 4- ilamina.

Ejemplo II- 193: Se preparó ácido 5- [- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofeno- 2- carboxílico siguiendo el procedimiento 3 comenzando a partir de 5- bromo- 3- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- ilamina y ácido 5- carboxitiofeno- 2- borónico.

Ejemplo II- 194: Se preparó {5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofen- 2- il)- (4- metil- piperazin- 1- il)- metanona siguiendo el procedimiento 4 comenzando a partir del ácido 5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofeno- 2- carboxílico y 4- metil- piperazin- 1- ilamina.

Ejemplos L- 1 a L- 176: se prepararon según el procedimiento 40. En la tabla 5, los compuestos son agrupados en secciones, con cada sección con una designación de letra. Los números de ejemplos son asignados de izquierda a derecha por filas. Por ejemplo, en la Sección A, los compuestos en la fila superior, de izquierda a derecha son los Ejemplos L- 1 a L- 4, y los compuestos en la segunda fila son, de izquierda a derecha, los Ejemplos L- 5- L- 8. El porcentaje de inhibición es el porcentaje de la inhibición c- MET a 50 nM.

Ejemplos L- 177 a L- 352 fueron preparados según el procedimiento 41. En la tabla 6, los compuestos son agrupados en secciones, con cada sección con una designación de letra. Los numeros de ejemplo son asignados de izquierda a derecha por filas. El porcentaje de inhibición es el porcentaje de la inhibición c- MET a 1 μM.

Ejemplos L- 353 a L- 548 se prepararon según el procedimiento 42. En la tabla 7, los compuestos son agrupados en secciones, cada sección con una designación de letra. Los números de ejemplo son asignados de izquierda a derecha por filas. El porcentaje de inhibición es el porcentaje de la inhibición c- MET a 1 μM.

Ejemplos L549 a L- 636 fueron preparados según el procedimiento 43. en la tabla 8, los compuestos son agrupados en secciones, con cada sección teniendo una designación de letra. Los números de ejemplo son asignados de izquierda a derecha mediante filas. El porcentaje de inhibición es el porcentaje de la inhibición c- MET a 1 μM.

EJEMPLOS BIOLÓGICOS

Se apreciará que, en cualquier serie dada de compuestos, un rango de actividades biológicas serán observadas. En sus aspectos actualmente preferidos, este invento se relaciona con compuestos novedosos capaces de modular, regular y/o inhibir la actividad de la proteinquinasa. Los siguientes ensayos se pueden emplear para seleccionar aquellos compuestos que demuestran el grado optimo de la actividad deseada.

Procedimientos de Ensayo

El siguiente ensayo *in vitro* puede ser utilizado para determinar el nivel de actividad y efecto de los diferentes compuestos del presente invento sobre una o más PKs. Ensayos similares se pueden diseñar a lo largo de las mismas líneas para cualquier PK utilizando técnicas bien conocidas en el estado de la técnica. Una referencia de literatura es proporcionada en (Technikova- Dobrova Z, Sardanelli AM, Papa S FEBS Lett. 1991 Nov 4; 292: 69- 72).

El procedimiento general es como sigue: compuestos y reactivos del ensayo de quinasa son introducidos en pozos de prueba. El ensayo es iniciado mediante la adición de la enzima quinasa. Los inhibidores de la enzima reducen la actividad medida de la enzima.

En el ensayo espectrofotométrico continuo- acoplado la producción de ADP dependiente de tiempo por la quinasa es determinada mediante análisis de la tasa de consumo de NADH mediante la medición de la disminución en absorbancia a 340 nm. Puesto que la Pk produce ADP este es reconvertido en ATP mediante reacción con piruvato de fosfoenol y piruvatoquinasa. El piruvato también es producido en esta reacción. El piruvato es subsecuentemente convertido en lactato mediante la reacción con deshidrogenasa de lactato, que simultáneamente convierte NADH a NAD. NADH tiene una absorbancia medible a 340 nm mientras NAD no.

El protocolo actualmente preferido para realizar los experimentos espectrofotométricos continuos acoplados para las PKs específicas es proporcionado a continuación. Sin embargo, la adaptación de este protocolo para determinar la actividad de los compuestos contra otras RTKs, así como también para CTKs y STKs, está dentro del alcance del conocimiento de aquellos con experiencia en el estado de la técnica.

Ensayo Espectrofotométrico HGFR acoplado- continuo

Este ensayo analiza la actividad de la tirosinaquinasa de HGFR sobre peptido de sustrato Met- 2, un peptido derivado del ciclo de activación de HGFR.

Materiales y Reactivos

1. Enzima HGFR proveniente de Upstate (Met, Activo) Cat. # 14- 526
2. Peptido Met- 2 (Ciclo de Activiación de HGFR) Ac- SRDMYDKEYYSVHNK (MW = 1960).

Disolver en 200 mM HEPES, pH 7.5 en concentración de 10 mM

3. 1M PEP (fosfo- enol- piruvato) en 200 mM HEPES 200 mM, pH 7.5
4. 100 mM NADH 100 (B- Nicotinamida Adenina Dinucleotido, Forma Reducida) en 200 mM HEPES, pH 7.5
5. 4M MgCL2 (Cloruro de Magnesio) en ddH2O
6. 1M DTT (Ditiotreitol) en 200 mM HEPES , pH 7.5
7. 15 Unidades/mL de LDH (Deshidrogenasa Láctica)
8. 15 Unidades/mL de PK (Pivuratoquinasa)

9. NaCl 5M disuelto en ddH2O
10. Solución Tween- 20 (calidad Protéico)
11. Amortiguador 1M HEPES: Sal de sodio del ácido (N- [2- Hidroxietil]piperazina- N- 2- etanosulfónico). Disolver en ddH2O, ajustar pH a 7.5, llevar volumen a 1L. Filtrar a 0.1 µm.
12. Agua calidad HPLC; Burdick y Jackson #365- 4, 1x4 litros (o equivalente)
13. DMSO a 100% (SIGMA)
14. Costar #3880 – placas negras de mitad de área de fondo plano para determinación de Ki y porcentaje de inhibición
15. Costar #3359 – placas de polipropileno de 96 pozos, fondo redondo para diluciones seriales
16. Costar #3635 – placas de fondo plano transparentes de placa UV para porcentaje de inhibición
17. Monturas de microcelda Beckman DU- 650 w/
18. Probeta de microcelda de 4 posiciones Beckman

Procedimiento:

Preparar Amortiguador de Dilución (DB) para Enzima (Para Preparación de 30 mL)

1. La concentración final DB es DTT 2 mM, NaCl2 25 mM, MgCl2 5 mM, Tween- 20 al 0.01%, y amortiguador 50 mM HEPES, pH 7.5.

2. Preparar 50 mM HEPES agregando 1.5 mL de HEPES 1M en 28.1 mL de ddH2O. Agregar el resto de los reactivos. En un frasco cónico de 50 mL, agregar 60 uL de DTT 1M, 150 uL de NaCl2, 150 uL de MgCl2 1M, y 30 uL de Tween- 20 al 10% para proporcionar el volumen total de 30 mL.

3. Vortex durante 5- 10 segundos

4. Retirar alícuotas de DB a 1 mL/tubo y rotular tubos como DB HGFR"

5. Nota: Este se puede preparar y almacenar antes de tiempo.

6. Congelar alícuotas sin utilizar en tubos de microcentrifuga a –20°C.

Preparación de Compuestos

1. Para placa de dilución de compuesto, agregar 4 uL de concentración 10 mM en la columna 1 de la placa, y llevar el volumen a 100 uL con DMSO a 100%.

4. Agregar 5 µL de DMSO para control negativo en la última columna de la placa de ensayo.
5. Mezclar con una pipeta multicanal o agitador orbital.
6. Pre- incubar durante 10 minutos a 37°C.
7. Agregar 10 µL de 500 HGFR 500 nM a cada pozo de la placa de pozos; la concentración HGFR final es 50 nM en un volumen final total de 100 µL.
8. Medir la actividad durante 10 minutos a $\lambda = 340$ nm y 37°C.

Los siguientes ensayos in vitro se pueden utilizar para determinar el nivel de actividad y efecto de los diferentes compuestos del presente invento sobre una o más PKs. Ensayos similares se pueden diseñar a lo largo de las mismas líneas para cualquier PK utilizando técnicas bien conocidas en el estado de la técnica.

Varios de los ensayos descritos en la presente son realizados en un formato ELISA (Ensayo con Inmunosorberte Ligado a Enzima) (Voller, 1980, "Ensayo con Inmunosorberte Ligado a Enzima," Manual de Inmunología Clínica, segunda edición, Rose y Friedman, Am. Soc. Of Microbiology, Washington, D.C., pp. 359-371). El procedimiento general es como sigue: un compuesto es introducido a células que expresan la quinasa de prueba, de manera natural o recombinante, durante un periodo de tiempo seleccionado después del cual, si la quinasa de prueba es un receptor, se agrega un ligando conocido que activa el receptor. En las células son sometidas a lisis y el lisado es transferido a los pozos de una placa ELISA previamente recubierta con un anticuerpo específico que reconoce el sustrato de la reacción de fosforilación enzimática. Componentes que no hacen parte del sustrato del lisado celular son lavados y la cantidad de fosforilación sobre el sustrato es detectada con un anticuerpo que reconoce específicamente la fosfotirosina al realizar comparación con células de control que no estuvieron en contacto con un compuesto de prueba.

Los protocolos actualmente preferidos para realizar los experimentos ELISA para PKs específicas son proporcionados a continuación. Sin embargo, la adaptación de estos protocolos para determinar la actividad de los compuestos contra otros receptores con actividad tirosinquinasa (RTKs), así como también para tirosinquinasas citoplásmicas (CTKs) y serina- treonina- tirosinaquinasas (STKs), está dentro del alcance de conocimiento de aquellos con experiencia en el estado técnica.

Otros ensayos descritos en la presente miden la cantidad de ADN elaborado en respuesta a la activación de una quinasa de prueba, la cual es una medida general de un respuesta proliferativa. El procedimiento general para este ensayo es como sigue: se introduce un compuesto a células que expresan la quinasa de prueba, ya sea de manera manual o recombinante, durante un periodo de tiempo seleccionado después del cual, si la quinasa de prueba es un receptor, se agrega un ligando conocido para activar el receptor. Después de incubación al menos durante la noche, se agrega un reactivo de rotulación de ADN tal como 5- bromodeoxiuridina (BrdU) o H3- thimidina. La cantidad de ADN rotulado es detectada ya sea con un anticuerpo anti- BrdU) o H3- timidina. La cantidad de ADN rotulado es detectada ya sea con un anticuerpo anti- BrdU o midiendo la radioactividad y es comparada con las células de control que no estuvieron en contacto con un compuesto de prueba.

ENSAYO DE TRANSFOSFORILACION MET

Este ensayo se utiliza para medir los niveles de fosfotirosina sobre un substrato poli(ácido glutamico:tirosina (4:1)) como un medio para identificar agonistas/antagonistas de transfosforilación met del substrato.

Materialcs y reactivos:

1. Placas Elisa Corning de 96 pozos, Corning Catálogo # 25805- 96.
2. Poly(glu, tyr) 4:1, Sigma, Cat. No; P 0275.
3. PBS, Catálogo Gibco # 450- 1300EB
4. HEPES 50 mM
5. Amortiguador Bloqueador: Disolver 25 g de Albumina de Suero Bovino, Sigma Cat. No A- 7888, en 500 ml de PBS, filtrar a través de un filtro de 4 µm.
6. Proteina de fusion GST purificada que contiene el dominio de la quinasa Met, Sugen, Inc.
7. Amortiguador TBST.
8. DMSO acuoso al 10% (MilliQue H_2O).
9. Adenosin- 5'- trifosfate (dH_2O) 10 mM acuoso, Sigma Cat. No. A- 5394.
10. Amortiguador de Dilución de Quinasa 2X: para 100 ml, mezclar 10 mL de HEPES 1M a pH 7.5 con 0.4 mL de BSA/PBS al 5%, 0.2 mL de

ortovanadato de sodio 0.1M y 1 mL de cloruro de sodio 5M en 88.4 mL de dH_2O.

11. Mezcla de Reacción ATP 4X: para 10 mL, mezclar 0.4 mL de cloruro de manganeso 1M y 0.02 mL de ATP 0.1 M en 9.56 mL de dH_2O.
12. Mezcla de controles negativos 4X: para 10 mL, mezclar 0.4 mL de cloruro de manganeso 1M en 9.6 mL de dH_2O.
13. Placas de polipropileno con fondo en V de 96 pozos NUNC, Catalogo Científico Aplicado # S- 72092
14. EDTA 500 mM.
15. Amortiguador de dilución de anticuerpos: para 100 mL, mezclar 10 mL de BSA/PBS al 5%, 0.5 mL de leche instantánea Carnation® al 5% en PBS y 0.1 mL de ortovanadato de sodio 0.1M en 88.4 mL de TBST.
16. Anticuerpo antifosfotirosina policlonal de conejo, Sugen, Inc.
17. Anticuerpo conjugado de peroxidasa de pepino picante anticonejo de cabra, Biosource, Inc.
18. Solución ABTS Solución: para 1 L, mezclar 19.21 g de ácido cítrico, 35.49 g Na_2HPO_4 y 500 mg de ABTS con suficiente dH_2O para preparar 1 L.
19. ABTS/H_2O_2: mezclar 15 mL de solución ABST con 2µL de H_2O_2 cinco minutos antes de utilizar.
20. 0.2 M
21.

Procedimiento:

1. Recubrir las placas ELISA con 2 µg de Poly(Glu- Tyr) en 100 µL de PBS, almacenar durante la noche a 4 ° C.
2. Bloquear la placa con 150 µL de BSA al 5%/ PBS durante 60 min.
3. Lavar la placa dos veces con PBS, una vez con amortiguador Hepes 50 mM pH 7.4.
4. Agregar 50 µl de la quinasa diluida a todos los pozos. (La quinasa purificada es diluida con Amortiguador de Dilución de quinasa. La concentración final debe ser 10 ng/pozo.)
5. Agregar 25 µL del compuesto de prueba (en DMSO al 4%) o DMSO solo (4% en dH_2O) para controles a la placa.

6. Incubar la mezcla de quinasa/compound durante 15 minutos.
7. Agregar 25 µL de $MnCl_2$ 40 mM a los pozos de control negativo.
8. Agregar 25 µL de la mezcla ATP/ $MnCl_2$ a los demás pozos (excepto los controles negativos). Incubar for 5 min.
9. Agregar 25 µL de EDTA 500 mM para detener la reacción.
10. Lavar placa 3x con TBST.
11. Agregar 100 µL de anti- Ptyr policlonal conejo diluido 1:10,000 en Amortiguador de dilución de anticuerpos a cada pozo. Incubar con agitación, a temperatura ambiente durante una hora.
12. Lavar placa 3x con TBST.
13. Diluir anticuerpo anti- conejo conjugado Biosource HRP 1: 6,000 en Amortiguador de dilución de anticuerpos. Agregar 100 µL por pozo e incubar a temperatura ambiente, con agitación, durante una hora.
14. Lavar placa 1X con PBS.
15. Agregar 100 µl de Solución ABTS/H2O2 a cada pozo.
16. Si es necesario, detener el desarrollo de la reacción con la adición de 100 µl de 0.2M HCl 0.2M por pozo.
17. Leer la placa sobre un lector ELISA Dynatech MR7000 con el filtro de prueba a 410 nM y el filtro de referencia a 630 nM.

ENSAYOS DE INCORPORACION DE BRDU

Los siguientes ensayos utilizan células diseñadas para expresar un receptor seleccionado y luego evaluar el efecto de un compuesto de interes sobre la actividad de síntesis de ADN inducida por ligandos mediante la determinación de incorporación de BrdU en el ADN.

Los siguientes materiales, reactivos y procedimiento son generales para cada uno de los siguientes ensayos de incorporación de BrdU. Se observan varianzas en ensayos específicos.

<u>Materiales y reactivos:</u>

1. El ligando apropiado.
2. Las células diseñadas apropiadas.

3. Reactivo de Rotulación BrdU: 10 mM, en PBS (pH 7.4)(Boehringer Mannheim, Alemania).
4. FixDenat: solución fijadora (lista para utilizar)(Boehringer Mannheim, Alemania).
5. Anti- BrdU- POD: anticuerpo monoclonal de ratón conjugado con peroxidasa (Boehringer Mannheim, Alemania).
6. Solución de substrato TMB: tetrametilbenzidina (TMB, Boehringer Mannheim, Germany).
7. Solución de lavado PBS : PBS 1X, pH 7.4.
8. Albumina Bovina (BSA), polvo en fracción V (Sigma Chemical Co., USA).

Procedimiento general:

1. Las células son sembradas a 8000 células/pozo en CS al 10%, Gln 2 mM en DMEM, en una placa 96 pozos. Las células son incubadas durante la noche a 37°C en CO_2 al 5%.
2. Después de 24 horas, las células son lavadas con PBS, y luego son despojadas de suero en medio libre de suero (CS al 0% en DMEM con BSA al 0.1%) durante 24 horas.
3. El tercer día, 25 ul que contiene ligando (preparado a 1 ug/ml en RPMI con BSA al 0.1%; la concentración HGF final es 200 nG/ml) y los compuestos de prueba son agregados a las células de manera simultanea. Los pozos de control negativo reciben DMEM libre de suero con BSA al 0.1% solamente; las células de control positivo reciben el ligando pero no el compuesto de prueba. Los compuestos de prueba son preparados en DMEM libre de sucro con ligando en una placa de 96 pozos, y diluidos de manera serial para 7 concentraciones de prueba.
4. Después de 18 horas de activación de ligandos, el reactivo de rotulación BrdU diluido (1:100 en DMEM, BSA al 0.1%) es agregado y las células son incubadas con BrdU (concentración final = 10 µM) durante 1.5 horas.
5. Despues de la incubación con reactivo de rotulación, el medio es retiro mediante decantación y tocando la placa invertida sobre papel toalla. Se

agrega solución FixDenat (50 µl/pozo) y las plates son incubadas a temperatura ambiente durante 45 minutos sobre un agitador de placa.

6. La solución FixDenat es completamente retirada mediante decantación y tocando la placa invertida sobre papel toalla. Se agrega leche (leche deshidratada al 5% en PBS, 200 µl/pozo) como una solución bloqueador y la placa es incubada durante 30 minutos a temperatura ambiente sobre un agitador de placa.
7. La solución bloqueadora es retirada mediante decantación y los pozos son lavados una vez con PBS. Se agrega solución Anti- BrdU- POD (1:200 dilución en PBS, 1% BSA) (50 µl/pozo) y la placa es incubada durante 90 minutos a temperatura ambiente sobre un agitador de placa.
8. El conjugado de anticuerpo es completamente retirado mediante decantación y elevando los pozos 5 veces con PBS, y la placa es secada invirtiendo y tocando la placa sobre papel toalla.
9. La solución de substrato TMB es agregada (100 µl/pozo) e incubada durante 20 minutos a temperatura ambiente sobre un agitador de placa hasta que el desarrollo de color es suficiente para detección fotométrica.

La absorbancia de las muestras es medida a 410 nm (en modo de "longitud de onda dual" con una lectura de filtro a 490 nm, como longitud de onda de referencia) sobre un lector de placa ELISA Dynatech.

Ensayo de Incorporación de BrdU HGF- inducido

Materiales y reactivos:

1. HGF Recombinante humano (Catátolo. No. 249- HG, R&D Sistemas, Inc. USA).
2. Células BxPC- 3 (ATCC CRL- 1687).

Procedimiento:

1. Células son sembradas a 9000 células/pozo en RPMI FBS al 10% en una placa de 96 pozos. Las células son incubadas durante la noche a 37°C en CO_2 al 5%.

2. Después de 24 horas, las células son lavadas con PBS, y luego son despojadas de suero en 100 µl de medio libre de suero (RPMI con BSA al 0.1% BSA) durante 24 horas.
3. El tercer día, se agregan 25 µl de ligando (preparado a 1 µg/ml en RPMI con BSA al 0.1%; concentración final de HGF es 200 mg/ml) y compuestos de prueba a las células. Los pozos de control negativo reciben 25 µl de RPMI libre de suero con BSA al 0.1% solamente; las células de control positivo reciben el ligando (HGF) pero no el compuesto de prueba. Los compuestos de prueba son preparados a 5 veces su concentración final en RPMI libre de suero con ligando en una placa de 96 pozos, y serialmente diluidos para proporcionar 7 concentraciones de prueba. Típicamente la concentración final más alta del compuesto de prueba es 100 µM, y se utilizan diluciones 1:3 (es decir, el rango de concentración final del compuesto de prueba es 0.137-100 µM).
4. Después de 18 horas de activación de ligandos, 12.5 µl de reactivo de rotulación BrdU diluido (1:100 en RPMI, BSA al 0.1%) es agregado a cada pozo y las células son incubadas con BrdU (la concentración final es 10 µM) durante 1 hora.
5. Igual que el procedimiento general.
6. Igual que el procedimiento general.
7. La solución bloqueadora es retirada mediante decantación y los pozos son lavados una vez con PBS. Solución anti- BrdU- POD (dilución 1:100 en PBS, BSA al 1%) es agregada (100 µl/pozo) y la placa es incubada durante 90 minutos a temperatura ambiente sobre un agitador de placa.
8. Igual que Procedimiento general.
9. Igual que Procedimiento general.
10. Igual que Procedimiento general.

MODELOS ANIMALES DE XENOINJERTO

La capacidad de los de los tumores humanos para crecer como xenoinjertos en ratones atímicos (*ej.*, Balb/c, nu/nu) proporciona un modelo in vivo útil para estudiar la

respuesta biológica a terapias para tumores humanos. Debido al primer xenotransplante exitoso de tumores humanos en ratones atímicos,(Rygaard y Povlsen, 1969, Acta Pathol. Microbial. Scand. 77:758- 760), muchas líneas celulares de tumores humanos diferentes (ej., mamaria, pulmonar, genitourinaria, gastrointestinal, de cabeza y cuello, glioblastoma, ósea, y de melanomas malignos) han sido trasplantadas y exitosamente cultivadas en ratones desnudos. Los siguientes ensayos se pueden utilizar para determinar el nivel de actividad, especificidad y el efecto de los diferentes compuestos del presente invento. Tres tipos generales de ensayos son útiles para evaluar los compuestos: es celular/ catalítico, celular/biológico y in vivo. El objetivo de los ensayos celulares/catalíticos es determinar el efecto de un compuesto sobre la capacidad de una TK para fosforilar tirosina sobre un substrato conocido en una celula. El objetivo de los ensayos celulares/biológicos es determinar el efecto de un compuesto sobre la respuesta biológica estimulada por una TK en una celula. El objetivo de los ensayos in vivo es determinar el efecto de un compuesto en un modelo animal de un trastorno particular como el cáncer.

Líneas celulares apropiadas para experimentos de xenoinjerto subcutáneo incluyen células C6 (glioma, ATCC # CCL 107), células A375 (melanona, ATCC # CRL 1555), células Calu 6 (pulmón, ATCC # HTB 56), células PC3 (prostata, ATCC # CRL 1435), células SKOV3TP5 y fibroblastos NIH 3T3 genéticamente diseñados para sobreexpresar EGFR, PDGFR, IGF- 1R o cualquier otra kinasa de prueba. El siguiente protocolo se puede utilizar para realizar experimentos de xenoinjerto:

Ratones atímicos hembra (BALB/c, nu/nu) son obtenidos en los Laboratorios Simonsen (Gilroy, CA). Todos animales son mantenidos bajo condiciones higienicas en jaulas Micro- aislantes con lechos Alfa- dri. Éstos reciben comida estéril para roedores y agua a discreción.

Las líneas celulares son cultivadas en medio apropiado (por ejemplo, MEM, DMEM, Ham's F10, o Ham's F12 más suero bovino fetal al 5% - 10% (FBS) y glutamina 2 mM (GLN)). Todos los medios de cultivo celular, la vitamina y suero bovino fetal son obtenidos en Gibco Life Technologies (Grand Island, NY) a menos que se especifique lo contrario. Todas las células son cultivadas en una atmósfera húmeda de 90- 96% aire y 5- 10% CO2 a 37°C. todas las líneas celulares son rutinariamente subcultivadas dos veces por semana y son negativas para micoplasma tal como se determinó mediante el método Mycotect (Gibco).

Las células son cosechadas en confluencia o en confluencia próxima con Tripsina- EDTA al 5% y pelctizadas a 450 x g durate 10 minutos. Los pellets son resuspendidos en PBS estéril o medio (sin FBS) hasta una concentración particular y las celulas son implantadas en en el costado trasero de los ratones (8- 10 ratones por grupo, 2- 10 x 10 6 células/animal). El crecimiento tumoral es medido durante tres a seis semanas utilizando calibradores Venier. Los volumenes tumorales son calculados como un producto de longitud x anchura x altura a menos que se indique lo contrario. Los valores P son calculados utilizando la prueba- t de Students. Los compuestos de prueba en 50 - 100 uL de excipiente (DMSO), VPD:D5W) se pueden liberar mediante inyección IP diferentes concentraciones comenzando generalmente un día después del implante.

Fosforilización Met –Ensayo Celular

Materiales y Reactivos

1. Placas de cultivo de 10 cm Falcon
2. Células de carcinoma de pulmón A549
3. Medio de crecimiento F12K (con FBS al 2% + glutamina 2mM)
4. Medio de Ensayo F12K (BSA al 0.1%).
5. Raspadores celulares Fisher.
6. Amortiguador de lisis (HNTG, ortovanidato de sodio 1 mM, PMSF 1 mM y fluoruro de sodio 2 mM)
7. Tubos Eppendorf de 1.5 mL.
8. Microcentrifuga Eppendorf.
9. Reactivos de ensayo BCA A y B (#23223 y 23224, Pierce).
10. Rotador de tubos de muestra.
11. Rotador de recipientes gel blot.
12. Amortiguador de muestra 5X.
13. Geles de acrilamida al 8% de tris- glicina pre- molde Novez
14. Cámara de electroforesis Bio- Rad
15. Amortiguador SDS- PAGE.
16. TBS (pH 7.6) + Triton X- 100 al 0.1% (TBST), con y sin leche al 5%.
17. Amortiguador de transferencia de Western blot
18. Papel de nitrocelulosa Osmonics
19. Papel Transblot Bio- Rad.

20. Aparato de transferencia de gel.
21. Anti- fosfotirosina (monoclonal de ratón).
22. Estándares pre- teñidos de Caleidoscopio Bio- Rad (161- 0324).
23. policlonal de conejo anti- g- met (c- 28), conjugado y no conjugado con agarosa (#sc- 161 AC y sc- 161, Santa Cruz Biotechnology, Inc.)
24. Ig- HRP de asno y anti- conejo (NA 934, Amersham).
25. Ig- HRP anti- conejo (NA 931, Amersham).
26. Sustrato Quimiluminicente SuperSignal West Pico (~34080, Pierce).
27. Saran Wrap (papel plástico de envoltura)
28. Casete de exposición Kodak BioMax
29. Pelicula de rayos X Fuji
30. Desarrollador de película Kodak.

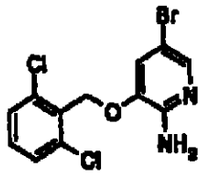
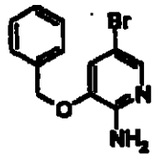
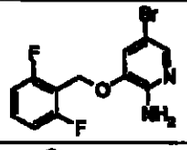
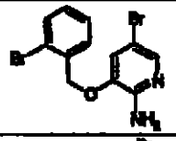
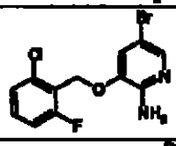
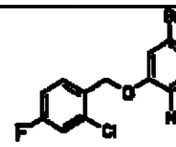
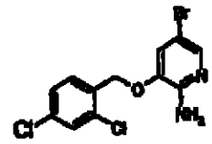
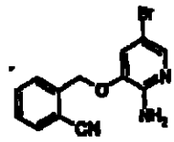
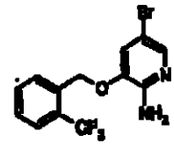
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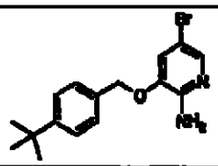
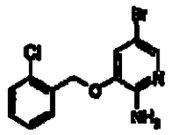
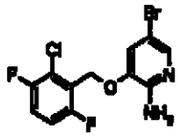
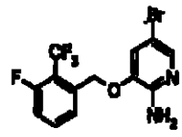
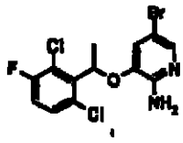
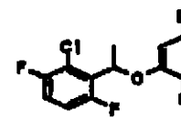
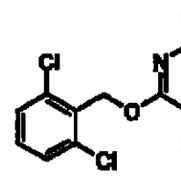
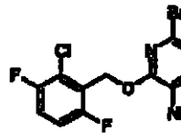
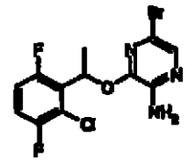
1. Colocar células en platos de 10 cm con medio de crecimiento con FBS al 2% + glutamina 2 mM. Crecer hasta lograr casi confluencia.
2. Privar de suero las células durante la noche en medio de ensayo con BSA al 1%.
2. Agregar fármaco a las placas, una dosis por placa, usualmente en una titulación de 2- flod. Agregar medio de ensayo (con la misma concentración DMSO que los fármacos) para aquel que no tenga fármaco.
3. Incubar las placas 4- 5 horas con el fármaco, luego agregar HG, 50 ng/mL duante 10 minutos.
4. Lavar las placas una vez con PBS, agregar 400 µl de amortiguador de lisis, y raspar las células. Recolectar en tubos tubos Eppendorf de 1.5 mL.
5. Después de 10- 20 minutos en el amortiguador de lisis, centrifugar los lisatos en una microcentrifuga a plena velocidad (14.000g) y recolectar los sobrenadantes en un tubo Eppendorf separado
6. Determinar la concentración protéica con los reactivos de ensayo BAC.
7. Ajustar la concentración de muestra a 0.5 mg de proteina en 0.4 mL utilizando amortiguador de lisis.
8. Agregar 15µl de anti- h- met AC para inmunoprecipitación, rotar las muestras durante 2 horas a 4°C.

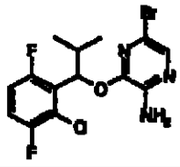
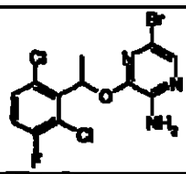
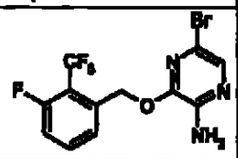
9. Lavar las muestras 3 veces con amortiguador de lisis y resuspender en 35 µl de amortiguador de muestras 5X.
10. Bullir la muestra a 100°C durante 10 minutos y microcentrifugar a alta velocidad para peletizar perlas de agarosa.
11. Cargar 15 µl a dos geles, uno para anti- fosforilación y el otro para anti- h-met. También cargar 10 µl de estándares pretefiidos, una pista por gel.
12. Correr gel alrededor de 100- 125 V, luego transferir gel a nitrocelulosa ya sea durante la noche a 70 mAmps o 1 hora a 500 aAmps.
13. Bloquear membranas sobre el rotador durante 1 hora en TBS + Triton X-100 a 0.1% (TBST) + PBS al 5%. Todos los pasos a partir de este punto son a temperatura ambiente a menos que se indique lo contrario.
14. Agregar 0.8 µg/ml de antifosfotirosina y 0.25 µg/mL de anti- h- met sobre rotador ya sea durante 2 horas o durante la noche.
15. Lavar las membranas 3 veces 5 minutos cada una en TBST sobre el rotador.
16. Agregar anticuerpos HRP- conjugados (anti- ratón oveja para las antifosfotirosina; anti- conejo de asno para el anti- h- met) a 1:5000 durante aproximadamente 45 minutos sobre el rotador.
17. Lavar las membranas 3 veces durante 5 minutos cada uno en TBST sobre el rotador.
18. Agregar los dos reactivos en el kit Supersignal juntos en volumenes iguales (3 mL + 3 mL para cada blot), rotar durante 1 –2 minutos.
19. Envolver los blots en Saran Wrap y cinta con seguridad al interior del casete de exposición.
20. En un cuarto oscuro con solo la luz de seguridad encendida, colocar una hoja de película dentro del casete. Después de un tiempo asignado, retirar la película y colocar en la maquina desarrolladora para procesamiento automático. Experimentar con tiempo de exposición para obtener la exposición apropiada.

TABLAS

Tabla I

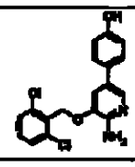
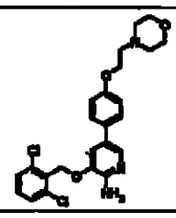
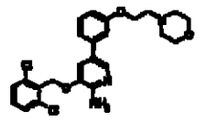
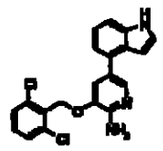
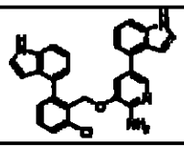
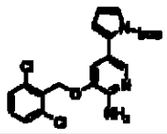
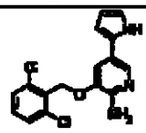
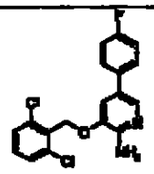
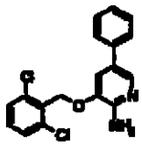
No	Estructura	Nombre	Met IC_{50} (nM)	^{1}H- NMR	MS m/z (M+1)
I(a)		5- Bromo- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina	5.3	(400 MHz, DMSO- d_6) δ 7.62 (m, 1H), 7.56 (m, 2H), 7.46 (m, 2H), 5.80 (s, 2H), 5.22 (s, 2H)	349
I(b)		3- Benciloxi- 5- bromo- piridin- 2- ilamina	>20	(400 MHz, DMSO- d_6) δ 7.56 (d, J =2 Hz, 1H), 7.47(d, J = 7.2 Hz, 2H), 7.38 (m, 2H), 7.32 (d, J = 7.2 Hz, 1H), 7.26 (d, J = 2 Hz, 1H), 5.95 (s, 2H), 5.14 (s, 2H)	280
I(c)		5- Bromo- 3- (2,6- difluoro- benciloxi)- piridin- 2- ilamina	40% a 20 µM	(400 MHz, DMSO- d_6) δ 7.60 (d, 1H), 7.52 (m, 1H), 7.40 (d, 1H), 7.18 (m, 2H), 5.81 (br. s. 2H), 5.12 (s, 2H)	315 (M+)
I(d)		5- Bromo- 3- (2- bromo- benciloxi)- piridin- 2- ilamina	>20	(400 MHz, DMSO- d_6) δ 7.65 (m, 2H), 7.60 (d, 1H), 7.42 (m, 2H), 7.30 (d, 1H), 5.94 (s, 2H), 5.13 (s, 2H)	357 (M+)
I(e)		5- Bromo- 3- (2- cloro- 6- fluoro- benciloxi)- piridin- 2- ilamina	>20	(400 MHz, DMSO- d_6) δ 7.80- 7.30 (m, 5H), 5.80 (br s, 2H), 5.15 (s, 2H)	331
I(f)		5- Bromo- 3- (2- cloro- 4- fluoro- benciloxi)- piridin- 2- ilamina		(400 MHz, DMSO- d_6) δ 7.80- 7.20 (m, 5H), 5.95 (br s, 2H), 5.10 (s, 2H)	331
I(g)		5- Bromo- 3- (2,4- dicloro- benciloxi- piridin- 2- ilamina		(400 MHz, DMSO- d_6) δ 7.80- 7.50 (m, 5H), 6.20 (br s, 2H), 5.20 (s, 2H)	348
I(h)		2- (2- amino- 5- bromo- piridin- 3- iloximetil)- benzonitrilo		(400 MHz, DMSO- d_6) δ 7.90- 7.30 (m, 6H), 5.90 (br s, 2H), 5.20 (s, 2H)	304 (M+)
I(i)		5- Bromo- 3- (2- trifluorometil benciloxi)- piridin- 2- ilamina		(400 MHz, DMSO- d_6) δ 7.80- 7.30 (m, 6H), 6.00 (br s, 2H), 5.25 (s, 2H)	347

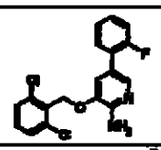
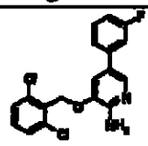
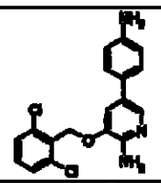
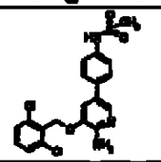
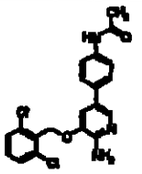
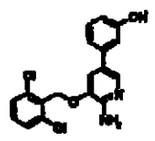
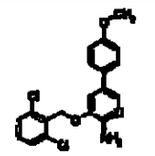
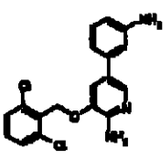
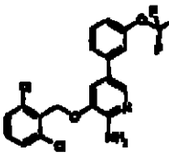
No	Estructura	Nombre	Met IC_{50} (μM)	^{1}H- NMR	MS m/z (M+1)
I(j)		5- Bromo- 3- (4- *tert*- butil- benciloxi)- piridin- 2- ilamina		(400 MHz, DMSO- d_6) δ 7.50- 7.20 (m, 6H), 5.85 (br s, 2H), 5.05 (s, 2H), 1.25 (s, 9H)	335 (M+)
I(H)		5- Bromo- 3- (2- cloro- benciloxi)- piridin- 2- ilamina		(400 MHz, DMSO- d_6) δ 7.70 - 7.20 (m, 6H), 5.90 (br s, 2H), 5.15 (s, 2H)	313
I(l)		5- Bromo- 3- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 2- ilamina		($CDCl_3$, 300 MHz) δ 4.7- 4.8 (brs, 2H), 5.21 (s, 2H), 7.03- 7.10 (dt, 1H, J 4.1, 9.1), 7.17- 7.25 (m, 2H), 7.75- 7.76 (d, J, 1.86).	
I(m)		5- Bromo- 3- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 2- ilamina			365
I(n)		5- Bromo- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina		($CDCl_3$, 300 MHz) δ 1.85- 1.95 (d, 3H), 4.7- 5.0 (brs, 2H), 5.9- 6.01 (q, 1H), 6.8- 6.95 (d, 1H), 7.01- 7.2 (t, 1H), 7.4- 7.45 (m, 1H), 7.8- 7.85 (d, 1H).	
I(o)		5- Bromo- 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 2- ilamina			364
II(a)		5- Bromo- 3- (2,6- dicloro- benciloxi)- pirazin- 2- ilamina		(400 MHz, DMSO- d_6 δ 5.45 (s, 2H), 6.45 (s, 2H), 7.50 (m, 3H), 7.63 (s, 1H)	350
II(b)		5- Bromo- 3- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- ilamina		(300 MHz, $CDCl_3$) δ 7.7 (s, 1H), 7.23- 7.16 (m, 1H), 7.09- 7,01 (m, 1H), 5.53 (s, 2H), 4.72 (s, 2H)	351
II(c)		5- Bromo- 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- ilamina		(400 MHz, DMSO- d_6) δ 1.75 (d, 3H), 6.26 (m, 1H), 6.46 (s, 2H), 7.28 (m, 1H), 7.41 (m, 1H), 7.52 (s, 1H)	365

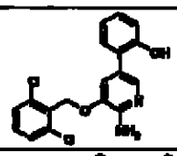
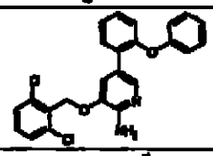
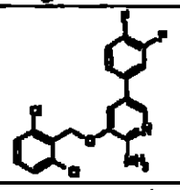
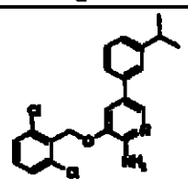
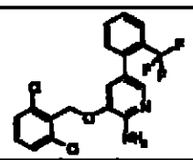
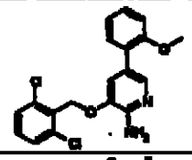
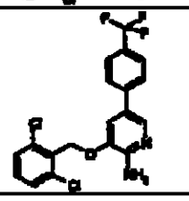
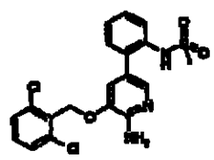
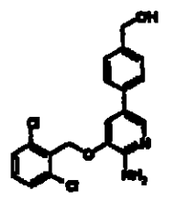
No	Estructura	Nombre	Met IC_{50} (μM)	^{1}H- NMR	MS m/z (M+1)
II(d)		5- Bromo- 3- [1- (2- cloro- 3,6- difluoro- fenil)- 2- metil- propoxi]- pirazin- 2- ilamina		(400 MHz, DMSO- d_6) δ 0.92 (d, 3H), 1.17(m, 3H), 2.57 (m, 1H), 5,75 (d, 1H), 6.49 (s, 2H), 7.24 (m, 1H). 7.40 (m, 1H), 7.54 (s, 1 H)	393
II(e)		5- Bromo- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- ilamina		(400 MHz, DMSO- d_6) δ 1.74 (d, 3H), 6.40 (m, 1H), 6.52 (br s, 2H), 7.30 (m, 1H), 7.48 (m, 1H), 7.56 (s, 1H); MS m/z 382 (M+1).	382
II(f)		5- Bromo- 3- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- ilamina			366

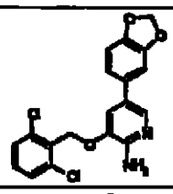
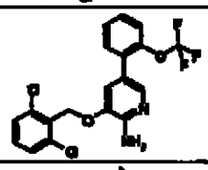
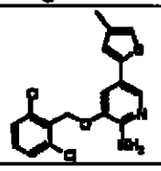
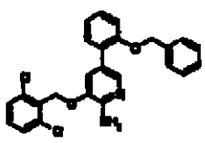
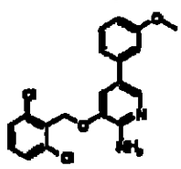
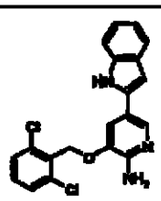
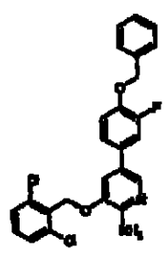
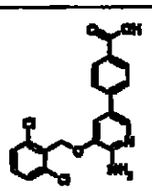
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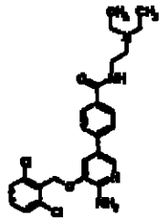
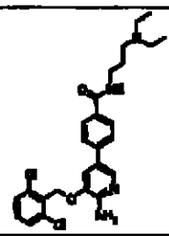
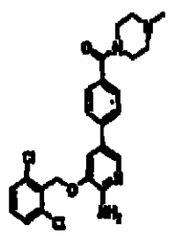
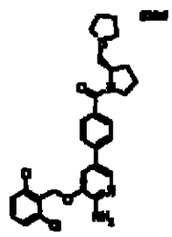
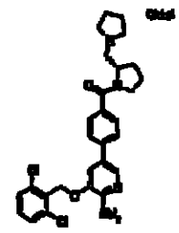
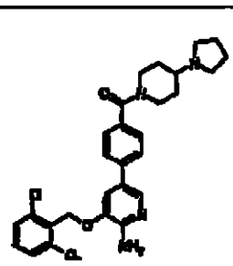
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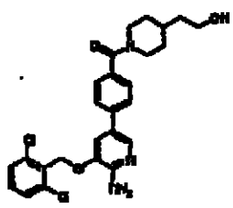
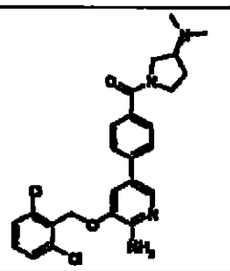
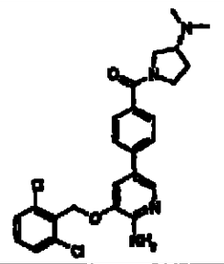
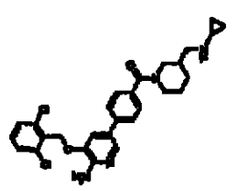
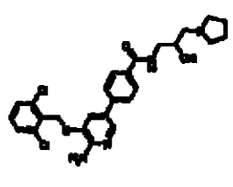
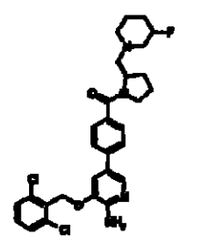
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I-1		4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenol	0.279	Ver ejemplo	(400 MHz, DMSO- d_6) δ 9.36 (s, 1H, OH), 7.77 (s, 1H), 7.54 (d, *J* = 5.2 Hz, 2H), 7.43 (m 4H) 6.78 (d, *J* = 5.2 Hz, 2H), 5.49 (br. s, 2H, NH_2), 5.30 (s, 2H, CH_2).	362
I-2		3- (2,6- Dicloro- benciloxi)- 5 [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina	0.58	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.81 (d, J = 1.2 Hz, 1H), 7.53 (m, 3H), 7.48 (m, 3H), 6.97 (d, 2H), 5.53 (br. s, 2H, NH_2), 4.08 (t, 2H), 3.55 (t, 4H), 2.68 (t, 2H), 2.46 (t, 4H).	374
I-3		3- (2,6- Dicloro- benciloxi)- 5- [3- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina	0.59	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.89 (d, J = 1.2 Hz, 1H), 7.54 (d, J = 5.2 Hz, 2H), 7.51 (d, J = 1.2 Hz, 1H), 7.44 (dd, 1H), 7.28 (dd, 1H), 7.18 (m, 2H), 6.83 (dd, 1H), 5.65 (br. s, 2H), 5.33 (s, 2H), 4.12 (t, 2H), 3.55 (t, 6H), 2.68 (t, 2H), 2.46 (t, 2H)	475
I-4		3- (2,6- Dicloro- benciloxi)- 5- (1H- indol- 4- il)- piridin- 2- ilamina	1.4	Ver ejemplo	(400 MHz, DMSO- d_6) δ 11.18 (s, 1H, NH), 7.87 (d, 1H), 7.5 (d, 2H), 7.46 (d, 2H), 7.36 (m, 1H), 7.33 (m, 1H), 7.12 (t, 1H), 7.03 (d, 1H), 6.49 (d, 1H), 5.61 (br. s, 2H, NH_2), 5.31 (s, 2H, CH_2).	384
I-5		3- [2- cloro- 6- (1H- indol- 4- il)- benciloxi]- 5- (1H- indol- 4- il)- piridin- 2- ilamina	4.71	Ver ejemplo		465
I-6		Terbutil ester del ácido 2- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- pirrol- 1- carboxílico	>20	Ver ejemplo		435
I-7		3- (2,6- dicloro- benciloxi)- 5- (1H- pirrol- 2- il)- piridin- 2- ilamina	4.25	Ver ejemplo	(400 MHz, DMSO- d_6) δ 11.05 (s, 1H), 7.85 (s, 1H), 7.58 (s, 1H), 7.55 (s, 1H), 7.50 (m, 2H), 6.75 (s, 1H), 6.35 (s, 1H), 6.05 (s, 1H), 5.50 (br. s, 2H), 5.30 (s, 2H).	335
I-8		3- (2,6- dicloro- benciloxi)- 5- (4- fluoro- fenil)- piridin- 2- ilamina	8.01	Ver ejemplo	(400 MHz, DMSO.d_6) δ 7.89 (s, 1H), 7.69 (m, 2H), 7.58 (m, 3H), 7.48 (m, 1H), 7.23 (m, 2H), 5.70 (br. s, 2H), 5.35 (s, 2H).	364
I-9		3- (2,6- dicloro- benciloxi)- 5- fenil- piridin- 2- ilamina	3.9	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.89 (d, J = 2 Hz, 1H), 7.63 (d, J = 6.8 Hz, 2H), 7.57 (d, J = 2 Hz, 1H), 7.54 (m, 2H), 7.43 (m, 1H), 7.40 (m, 2H), 7.26 (m, 1H), 5.68 (br. s, 2H), 5.34 (s, 2H).	345

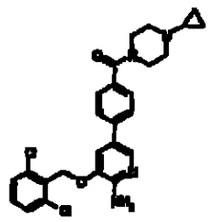
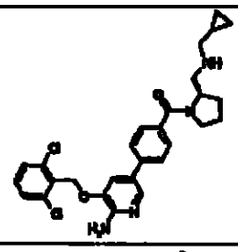
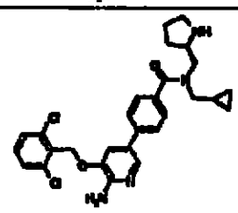
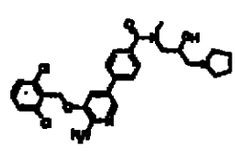
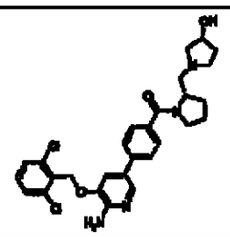
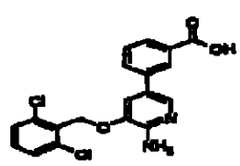
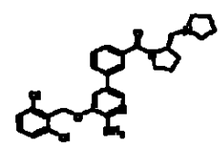
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 10		3- (2,6- Dicloro- benciloxi)- 5- (2- fluoro- fenil)- piridin- 2- ilamina	6.09	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.76 (d, 1H), 7.55 (m, 2H), 7.54 (m 1H), 7.46 (m, 2H), 7.32 (m, 1H), 7.25 (m, 2H), 5.78 (br. s, 2H), 5.28 (s, 2H).	364
I- 11		3- (2,6- Dicloro- benciloxi)- 5- (3- fluoro- fenil)- piridin- 2- ilamina	13.8	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.95 (d, 1H), 7.58- 7.44 (m, 7H), 7.17 (m 1H), 5.78 (br. s, 2H), 5.35 (s, 2H).	364
I- 12		5- (4- amino- fenil)- 3- (2,6- dicloro- benciloxi)- piridin- 2 ilamina	0.606	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.75 (d, 1H), 7.54 (dd, 4H), 7.47 (m, 1H), 7.40 (d, 1H), 7.29 (dd, 2H), 6.60 (dd, 2H), 5.44 (br. s, 2H), 5.31 (s, 2H), 5.15 (br s, 2H).	360
I- 13		N- {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- metanosulfonamida	0.44	Ver ejemplo	(400 MHz, DMSO- d_6) δ 9.70 (s, 1H), 7.86 (d, 1H), 7.59 (m, 1H), 7.56 (m, 2H), 7.55 (m, 1H), 7.45 (m, 2H), 7.22 (dd, 2H), 5.63 (br. s, 2H), 5.33 (s, 2H), 2.95 (s, 3H).	439
I- 14		N- {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- acetamida	>20	Ver ejemplo	(400 MHz, DMSO- d_6) δ 9.94 (s, 1H), 7.86 (d, 1H), 7.59 (m, 1H), 7.57 (m, 2H), 7.54 (m, 2H), 7.48 (m, 2H), 5.61 (br. s, 2H), 5.33 (s, 2H), 2.04 (s, 3H).	402
I- 15		3- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenol	1.34	Ver ejemplo	400 MHz, DMSO- d_6) δ 7.83 (s, 1H), 7.55 (dd, 2H), 7.46 (m 2H), 7.19 (m, 1H), 7.10 (m, 1H), 7.04 (m, 1H), 6.98 (m, 1H), 6.69 (m, 1H), 5.67 (br. s, 2H), 5.33 (s, 2H).	360
I- 16		3- (2,6- Dicloro- benciloxi)- 5- (4- metoxi- fenil)- piridin- 2- ilamina	6.55	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.83 (s, 1H), 7.62- 7.54 (m, 4H), 6.97 (dd, 2H), 6.66 (dd, 2H), 5.58 (br. s, 2H), 5.33 (s, 2H), 3.77 (s, 3H).	357
I- 17		5- (3- amino- fenil)- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina	1.07	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.68 (m, 1H), 7.45 (m, 1H), 7.36 (t, 1H), 7.28 (d, 1H), 7.22 (m, 1H), 6.93 (d, 1H), 6.86 (d, 1H), 6.64 (dd, 1H), 5.34 (s, 2H), 4.73 (br s, 2H), 4.12 (br s, 2H).	360
I- 18		3- (2,6- dicloro- benciloxi)- 5- (3- trifluorometoxi- fenil)- piridin- 2- ilamina	>20	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.95 (d, 1H), 7.49- 7.24 (m, 7H), 7.17 (m, 1H), 5.39 (s, 2H), 4.81 (br s, 2H).	429

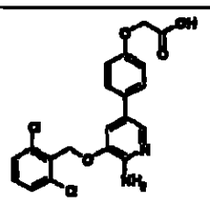
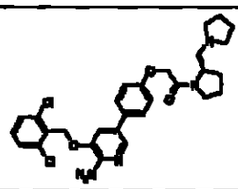
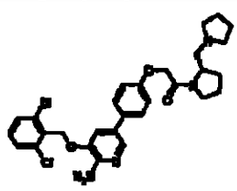
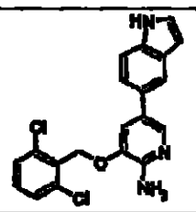
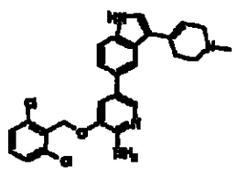
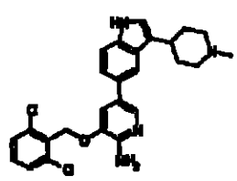
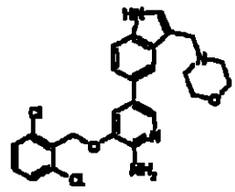
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 19		2- [6- amino- 5- (2,6- dicloro- bezenziloxi)- piridin- 3- il]- fenol	2.16	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.81 (d, 1H), 7.66 (m, 2H), 7.52 (m, 1H), 7.37 (d, 1H), 726 (m, 3H), 6.99 (m, 2H), 5.32 (s, 2H), 4.77 (br s, 2H)	361
I- 20		3- (2,6- dicloro- benciloxi)- 5- (2- fenoxi- fenil)- piridin- 2- ilamina	>20	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.88 (d, 1H), 7.66 (m, 2H), 7.45 (m, 3H), 7.34 (m, 2H), 7.26 (m, 3H), 7.07 (m, 2H), 6.93 (, 2H), 5.16 (s, 2H), 4.66 (br s, 2H).	437
I- 21		3- (2,6- dicloro- benciloxi)- 5- (3,4- difluoro- fenil)- piridin- 2- ilamina	14.3	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.89 (d, 1H), 7.40 (d, 2H), 7.26 (m, 5H), 5.37 (s, 2H), 4.80 (br s, 2H).	381
I- 22		3- (2,6- dicloro- benciloxi)- 5- (3- isopropil- fenil)- piridin- 2- ilamina	15.9	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, 1H), 7.40- 7.15 (m, 8H), 5.38 (s, 2H), 4.73 (br s, 2H), 2.98 (m, 1H), 1.31 (d, 6H).	387
I- 23		3- (2,6- dicloro- benciloxi)- 5- (2- trifluorometil- fenil)- piridin- 2- ilamina	>20	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.76 (d, J = 8.7 Hz, 1H), 7.69 (s, 1H), 7.58 (t, J = 7.3 Hz, 1H), 7.47 (t, J = 7.4 Hz, 1H), 7.38 (d, J =7.4 Hz, 2H), 7.27 (m, 2H), 7.17 (s, 1H), 5.29 (s, 2H), 4.78 (br s, 2H).	413
I- 24		3- (2,6- dicloro- benciloxi)- 5- (2- metoxi- fenil)- piridin- 2- ilamina	11.5	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.41- 7.24 (m, 6H), 7.02 (m, 2H), 5.32 (s, 2H), 4.69 (br s, 2H), 3.84 (s, 3H).	375
I- 25		3- (2,6- dicloro- benciloxi)- 5- (4- trifluorometil- fenil)- piridin- 2- ilamino	>20	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.98 (d, J = 1.8 Hz, 1H), 7.66 (m, 3H), 7.36 (m, 3H), 7.29 (m, 2H), 7.89 (s, 1H), 5.38 (s, 2H), 4.93 (br s, 2H).	413
I- 26		N- {2- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- metanosulfonamida	>20	Ver ejemplo	(300 MHz, $CDCl_3$) δ 8.75 (br s, 1H), 7.70- 7.14 (m, 9H), 5.31 (s, 2H), 5.16 (br s, 2H), 3.16 (s, 3H)	438
I- 27		{4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- metanol	2.5	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.84 (d, J = 1.8 Hz, 1H), 7.66 (m, 2H), 7.63- 7.18 (m, 6H), 5.36 (s, 2H), 4.75 (d, 2H), 4.73 (br s, 2H), 2.5 (br, 1H).	375

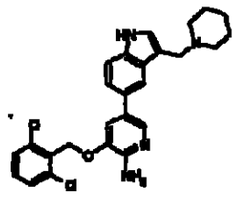
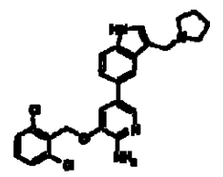
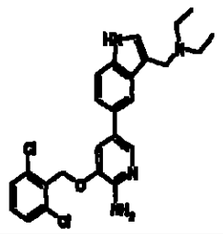
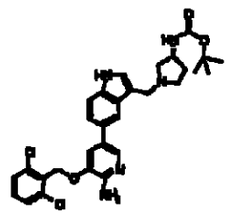
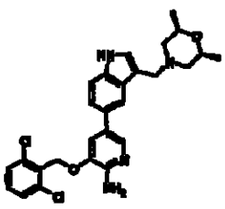
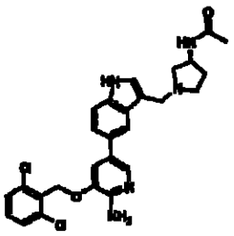
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 28		5- benzo)[1,3]dioxol- 5- il- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina	8.5	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.88 (d, J = 1.5 Hz, 1H), 7.37 (m, 2H), 7.29 (m, 2H), 6.99 (d, 2H), 6.87 (d, 1H), 5.99 (s, 2H), 5.36 (s, 2H), 4.74 (br s, 2H).	389
I- 29		3- (2,6- dicloro- benciloxi)- 5- (2- trifluorometoxi- fenil)- piridin- 2- ilamina	>20	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.47- 7.25(m, 8H), 5.33 (s, 2H), 4.82 (br s, 2H).	429
I- 30		3- (2,6- dicloro- benciloxi)- 5- (4- metil- tiofen- 2- il)- piridin- 2- ilamina	3.5	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.9 Hz, 1 H), 7.37 (d, J = 8.5 Hz, 2H), 7.29 (m, 2H), 7.00 (d, J = 1.1 Hz, 1H), 6.80 (s, 1H), 5.34 (s, 2H), 4.80 (br s, 2H), 2.28 (s, 3H).	365
I- 31		5- (2- benciloxi- fenil)- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina	>20	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.90 (d, J = 1.7 Hz, 1H), 7.49 (d, J = 1.7 Hz, 1H), 7.31 (m, 10H), 7.06 (m, 2H), 5.06 (s, 2H), 4.77 (br s, 2H).	451
I- 32		3- (2,6- dicloro- benciloxi)- 5- (3- metoxi- fenil)- piridin- 2- ilamina	4.01	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.7 Hz, 1H), 7.39- 7.11 (m, 4H), 7.13 (d, J = 7.7 Hz, 2H), 7.07 (t, J = 2.1 Hz, 1H), 6.88 (dd, J = 8.2 Hz, 2.1 Hz, 1H), 5.36 (s, 2H), 4.78 (br s, 2H), 3.87 (s, 3H).	375
I- 33		3- (2,6- dicloro- benciloxi)- 5- (1H- indol- 2- il)- piridin- 2- ilamina	7.5	Ver ejemplo	(300 MHz, $CDCl_3$) δ 8.47 (br s, 1H), 8.04 (s, 1H), 7.70 (d, J = 5.5 Hz, 1H), 7.62- 7.11 (m, 6H), 6.71 (d, J = 1.3 Hz, 1H), 6.66 (dd, J = 7.7 Hz, 2.1 Hz, 1H), 5.29 (s, 2H), 4.73 (br s, 2H).	384
I- 34		5- (4- benciloxi- 3- fluoro- fenil)- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina	13.5	Ver ejemplo	(400 MHz, DMSO- d_6) δ 5.20 (s, 2H), 5.32 (s, 2H), 5.65 (s, 2H), 7.25 (t, 1H), 7.33 (m, 1H), 7.39 (m, 3H), 7.46 (m, 3H), 7.51 (m, 4H), 7.88 (s, 1H).	469
I- 35		ácido 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}benzoico	12.8	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.98 (s, 1H), 7.92 (d, J = 5.6 Hz, 2H), 7.75 (d, J = 4.8 Hz, 2H), 7.55 (d, J = 5.2 Hz, 1H), 7.54 (dd, 2H), 7.45 (m, 1H), 5.8 (br. S, 2H), 5.34 (s, 2H).	390

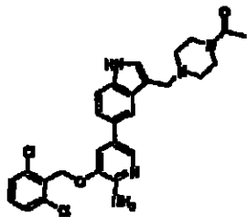
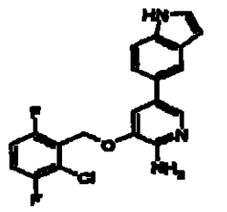
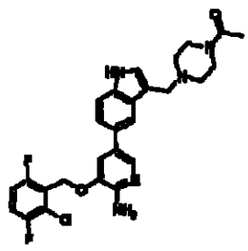
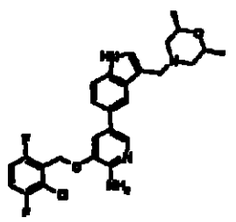
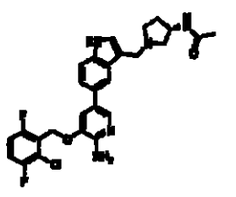
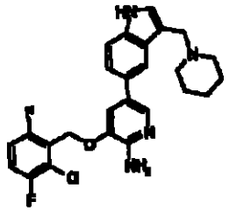
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 36		4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- N- (2- dietilamino- etil)- benzamida	0.99	Ver ejemplo	(400 MHz, DMSO- d_6) δ 8.45 (s, 1H), 7.97 (d, J = 1.2 Hz, 1H), 7.86 (d, J = 5.6 Hz, 2H), 7.73 (d, J = 5.6 Hz, 2H), 7.60 (d, J = 1.2 Hz, 1H), 7.54 (d, J = 5.2 Hz, 2H), 7.44 (dd, 1H), 5.77 (br. s, 2H), 5.34 (s, 2H), 3.3 (m, 4H), 2.6 (m, 4H), 0.99 (t, 6H).	487
I- 37		4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- N- (3- dietilamino- propil)- benzamida	0.82	Ver ejemplo	(400 MHz, DMSO- d_6) δ 8.60 (s, 1H), 7.95 (d, J = 1.2 Hz, 1H), 7.85 (d, J = 5.6 Hz, 1H), 7.75 (d, J = 5.6 Hz, 1H), 7.70 (d, J = 1.2 Hz, 1H), 7.60 (m, 1H), 7.55 (m, 2H), 7.45 (m, 2H), 5.70 (br. s, 2H), (s, 2H), 3.3 (m, 4H), 2.6 (m, 4H), 1.7 (m, 2H), 1.0 (t, 6H).	501
I- 38		{4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona	1.02	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.95 (d, J = 2Hz, 1H), 7.72 (dd, J = 6, 1.6 Hz, 2H), 7.59 (d, J = 1,6 Hz, 1H), 7.57 (d, J = 1.2 Hz, 1H), 7.55 (s, 1H), 7.43(dd, J = 6, 1.2 Hz, 1H), 7.40 (dd, J = 6, 1.6 Hz, 2H), 5.76 (br. s, 2H), 5.35 (s, 2H), 3.6 (m, 4H), 2.3(m, 4H), 2.2 (s, 3H).	471
I- 39		{4- (6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil }- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	0.062/ 0.11/0.2 (Hi 0.04)	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.96 (d, 1H), 7.72 (dd, 2H), 7.59 (m, 2H), 7.54 (m, 2H), 7.47 (m, 2H), 5.76 (br. s, 2H), 5.36 (s, 2H), 4.35 (m, 1H), 3.5 (d, 2H), 3.0 (m, 4H), 1.7- 2.0 (m, 10H).	525
I- 40		{4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	0.21	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.93 (d, 1H), 7.68 (dd, 2H), 7.57 (d, 1H), 7.54 (dd, 2H), 7.47 (m, 2H), 7.44 (m, 1H), 5.74 (br. s, 2H), 5.34 (s, 2H), 3.45 (m, 1H), 3.3 (m, 4H), 2.46 (m, 2H), 1.95 (m, 2H), 1.84 (m, 4H), 1.63 (m, 4H).	526
I- 41		{4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	0.35	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7,95 (d, 1H), 7.70 (dd, 2H), 7.55 (d, 1H), 7.48 (dd, 2H), 7.41 (m, 1H), 7.39 (m, 2H), 5.76 (br. s, 2H), 5.35 (s, 2H), 3.0 (m, 4H), 2.6 (m, 4H), 2.25 (s, 1H), 1.89 (m, 4H), 1.66 (m, 4H).	525

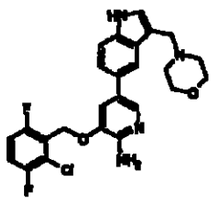
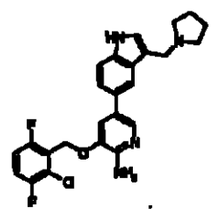
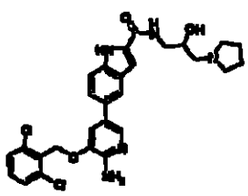
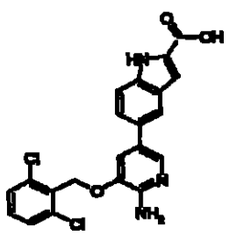
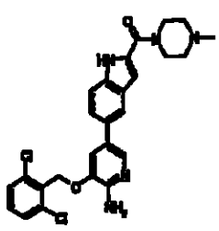
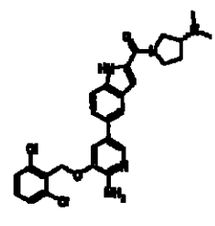
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 42		{4- [6- amino- 5- (2,6- diclorobenciloxi)- piridin- 3- il]- fenil}- [4- (2- hidroxi- etil)- piperidin- 1- il]- metanona	0.56	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.94 (d, 1H), 7.71 (dd, 2H), 7.70 (d, 1H), 7.59 (dd, 2H), 7.55 (m, 1H), 7.45 (m, 2H), 5.76 (br. s, 2H), 5.35 (s, 2H), 4.35 (t, 2H), 3.60 (m, 1H), 3.44 (m, 2H), 3.0 (m, 2H), 1.68 (m, 2H), 1.40 (m, 2H), 1.37 (m, 2H).	500
I- 43		{4- [6- amino- 5- (2,6- diclorobenciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona	0.47	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.95 (d, 1H), 7.75 (dd, 2H), 7.57 (d, 1H), 7.55 (dd, 2H), 7.48 (m, 1H), 7.46 (m, 2H), 5.76 (br. s, 2H), 5.35 (s, 2H), 3.60 (m, 1H), 3.0 (m, 2H), 2.2 (s, 3H), 2.1 (s, 3H), 1.15 (m, 2H).	485
I- 44		{4- [6- amino- 5- (2,6- diclorobenciloxi)- piridin- 3- il]- fenil}- [(3R)- 3- dimetilamino - pirrolidin- 1- il]- metanona	0.65	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.95 (m, 1H), 7.72 (m, 2H), 7.60 (m, 1H), 7.55 (m, 2H), 7.46 (m, 3H), 5.76 (br. s, 2H), 5.35 (s, 2H), 3.50 (m, 3H), 3.0 (m, 2H), 2.1 (s, 3H), 2.05 (s, 3H), 1.1 (m, 2H).	485
I- 45		{4- [6- amino- 5- (2,6- diclorobenciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- ciclopropilaminometil- piperidin- 1- il]- metanona	0.77	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.94 (d, 1H), 7.77 (m, 2H), 7.57 (m, 2H), 7.55 (m, 1H), 7.46 (dd, 1H), 7.39 (m, 2H), 5.79 (s, 2H), 5.35 (s, 2H), 4.4 (m, 1H), 3.6 (m, 1H), 2.6- 3.0 (m, 4H), 1.4- 1.8 (m, 8H), 0.8 (m, 2H).	526
I- 46		{4- [6- amino- 5- (2,6- diclorobenciloxi)- piridin- 3- il]- N- (2- hidroxi- 3- pirrolidin- 1- il- propil)benzamida	0.2	Ver ejemplo	(400 MHz, DMSO- d_6) δ 8.48 (m, 1H), 7.99 (d, 2H), 7.88 (m, 2H), 7.75 (m, 2H), 7.61 (d, 1H), 7.57 (m, 2H), 7.46 (dd, 1H), 5.79 (s, 2H), 5.36 (s, 2H), 4.8 (m, 1H), 3.75 (m, 1H), 3.44 (m, 1H), 3.18 (m, 1H), 2.53 (m, 4H), 2.40 (m, 1H), 1.67 (m, 4H)	515
I- 47		{4- [6- amino- 5- (2,6- diclorobenciloxi)- piridin- 3- il]fenil}- [(2S)- 2- (3- fluoro- piperidin- 1- ilmetil)- pirrolidin- 1- il]- metanona	0.42	Ver ejemplo		557

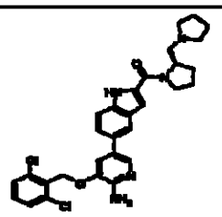
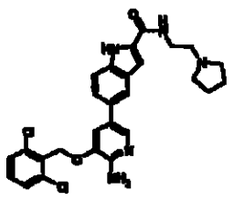
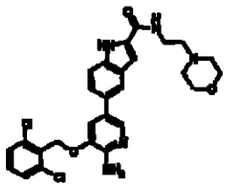
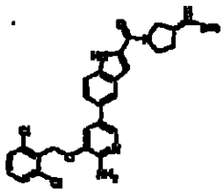
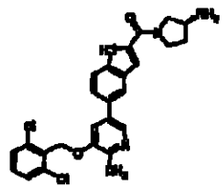
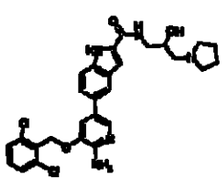
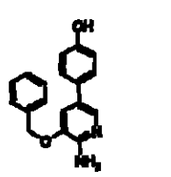
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 48		{4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]fenil }- (4- ciclopropil- piperazin- 1- il)- metanona	1.67	Ver ejemplo		497
I- 49		{4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]fenil }- {(2H)- 2- [ciclopropilmetil- amino)- metil }- pirrolidin- 1- il }- metanona	0.37	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.92 (d, 1H), 7.67 (m, 2H) 7.54 (m, 2H), 7.49 (m, 2H), 7.43 (m, 2H), 5.73 (s, 2H), 5.32 (s, 2H), 4.2 (m, 1H), 3.5 (m, 1H), 3.28 (m, 4H), 2.0- 1.7 (m, 6H), 1.18 (m, 4H)	525
I- 50		{4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- N- ciclopropilmetil- N- (2H)- pirolidin- 2- ilmetil- benzamida	0.29	Ver ejemplo	(400 MHz, DMSO- d_6) δ 8.16 (d, 1H), 7.61 (d, 1H), 7.38 (m, 2H), 7.23- 7.18 (m, 4H), 7.09 (m, 1H), 5.44 (s, 2H), 4.98 (s, 2H), 4.05 (m, 1H), 3.2 (m, 1H), 3.1 (m. 1H), 2.93 (m, 8H), 2.78 (m, 2H),2.10 (m, 4H).	525
I- 51		{4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- N- (2- hidroxi- 3- pirrolidin- 1- il- propil)- N- metil- benzamida	0.71	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.90 (m, 1H), 7.76 (m, 1H), 7.63 (m, 2H), 7.52(d, 2H), 7.50 (m, 2H), 7.40 (m, 1H), 5.69 (s, 2H), 5.30 (s, 2H), 3.70 (m, 1H), 2.96 (s, 3H), 2.44 (m, 4H), 2.34 (m, 4H), 1.75 (m, 4H).	529
I- 52		{4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]fenil }- {(2S)- 2- [(3R)- 3- hidroxi- pirrolidin- 1- ilmetil]- pirrolidin- 1- il }- metanona	0.53	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.96 (d, 1H), 7.70 (m, 2H), 7.60 (m, 1H), 7.57 (m, 1H), 7.55 (m, 3H), 7.46 (m, 1H), 5.78 (s, 2H), 5.37 (s, 2H), 4.3 (m, 1H), 3.6 (m, 4H), 3.2 (m, 4H), 1.9 (m, 4H), 1.24 (m, 4H).	541
I- 53		acido 3- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- benzoico	16	Ver ejemplo	(400 MHz, DMSO- d_6) δ 8.13 (m, 1H), 7.91 (d, 1H), 7.98 (m, 2H), 7.56 (dd, 2H), 7.54 (m, 2H), 7.47(m, 1H), 5.76 (s, 2H), 5.36 (s, 2H).	389
I- 54		{3- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil }- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	2.5	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.93 (d, 1H), 7.74 (m, 2H), 7.56 (m, 3H), 7.46 (m, 2H), 7.36 (m, 1H), 5.74 (s, 2H), 5.35 (s, 2H), 4.40 (m, 1H), 3.40 (d, 2H), 3.0 (m, 4H), 1,7- 2.0 (m, 10H)	525

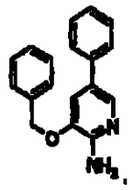
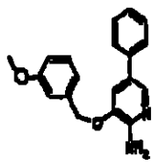
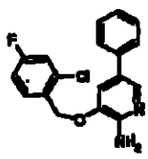
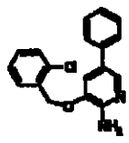
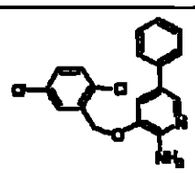
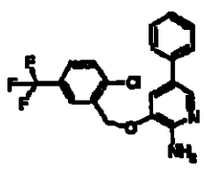
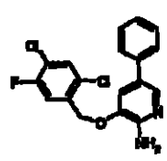
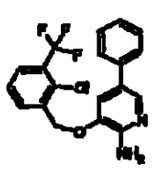
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 55		acido{4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenoxi} acetico	2.41	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.81 (d, 1H), 7.56 (m, 2H), 7.48 (m, 4H), 6.87 (m, 2H), 5.53 (s, 2H), 5.32 (s, 2H), 4.33 (s, 2H)	419
I- 56		2- {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenoxi}- 1- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- etanona	0.53	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.77 (d, 1H), 7.52 (d, 1H), 7.47 (m, 3H), 7.41 (m, 2H), 6.88 (m, 2H), 5.51 (s, 2H), 5.28 (s, 2H), 4.67 (s, 2H), 4.20 (m, 1H), 3.42 (m, 2H), 1.82 (m, 4H), 1.96 (m, 10H).	555
I- 57		2- {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3il]- fenoxi}- 1- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- etanona	0.5	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.82 (d, 1H), 7.57 (d, 1H), 7.52 (m, 3H), 7.45 (m, 2H), 6.93 (m, 2H), 5.56 (s, 2H), 5.33 (s, 2H), 4.72 (s, 2H), 4.20 (m, 1H), 3.5 (m, 2H), 2.52 (m, 6H), 1.85 (m, 4H), 1.66 (m, 4H)	555
I- 58		3- (2,6- dicloro- benciloxi)- 5- (1H- indol- 5- il)- piridin- 2- ilamina	4.3	Ver ejemplo	(400 MHz, DMSO- d_6) δ 11.05 (s, 1H, NH), 7.87 (d, 1H), 7.76 (m, 1H), 7.57 (m, 3H), 7.40- 7.48 (m, 2H), 7.34 (m, 2H), 6.44 (m, 1H), 5.49 (br. s, 2H, NH_2), 6.36 (s, 2H, CH_2)	384
I- 59		3- (2,6- dicloro- benciloxi)- 5- [3- (1- metil- 1,2,3,6- tetrahidro- piridin- 4- il)- 1H- indol- 5- il]- piridin- 2- ilamina	1.57	Ver ejemplo	(400 MHz, DMSO- d_6) δ 11.35 (d, 1H, NH), 7.95 (s, 1H), 7.89 (d, 1H), 7.55 (m, 4H), 7.45 (m, 2H), 7.39 (dd, 1H), 6.25 (m, 1H), 5.54 (br. s, 2H, NH_2), 5.37 (s, 2H, CH_2), 3.77 (m, 2H), 3.32 (m, 2H), 2.82 (m, 2H), 2.80 (s, 3H).	480
I- 60		3- (2,6- dicloro- benciloxi)- 5- [3- (1- metil- piperidin- 4- il)- 1H- indol- 5- il]- piridin- 2- ilamina	3.04	Ver ejemplo	(400 MHz, DMSO- d_6) δ 10.9 (d, 1H, NH), 7.90 (d, 1H), 7.80 (s, 1H), 7.55 (m, 4H), 7.46 (m, 2H), 7.32 (dd, 1H), 5.50 (br. s, 2H, NH_2), 5.38 (s, 2H, CH_2), 3.32 (m, 2H), 3.02 (m, 2H), 2.90 (m, 1H), 2.67 (s, 3H), 2.10 (m, 2H), 1.98 (m, 2H).	481
I- 61		3- (2,6- dicloro- benciloxi)- 5- (3- morfolin- 4- ilmetil- 1H- indol- 5- il)- piridin- 2- ilamina	1.19	Ver ejemplo	(400 MHz, DMSO- d_6) δ 2.31 (m, 4H), 3.55 (m, 4H), 3.66 (s, 2H), 5.26 (s, 2H), 5.45 (s, 2H), 7.22 (s, 1H), 7.34 (m, 2H), 7.48 (m, 2H), 7.57 (m, 2H), 7.80 (s, 1H), 7.85 (s, 1H), 10.92 (br s, 1H)	483

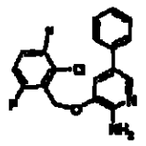
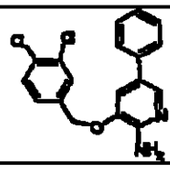
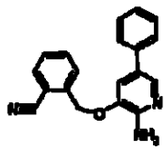
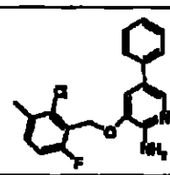
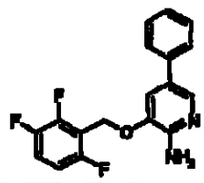
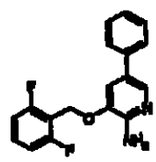
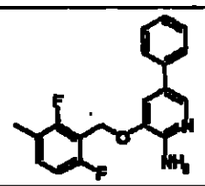
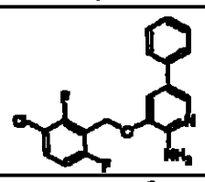
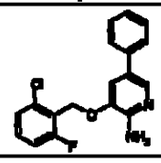
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 62		3- (2,6- dicloro- benciloxi)- 5- (3- piperidin- 1- ilmetil- 1H- indol- 5- il)- piridin- 2- ilamina	1.41	Ver ejemplo	(300 MHz, $CDCl_3$) δ 1.43 (m, 2H), 1.60 (m, 4H), 2.50 (m, 4H), 3.76 (s, 2H), 4.65 (br s, 2H), 5.40 (s, 2H), 7.19 (s, 1H), 7.27 (m, 1H), 7.38 (m, 5H), 7.87 (s, 1H), 8.01 (d, J = 1.7 Hz, 1H), 8.17 (br s, 1H)	481
I- 63		3- (2,6- dicloro- benciloxi)- 5- (3- pirrolidin- 1- ilmetil- 1H- indol- 5- il)- piridin- 2- ilamina	1.34	Ver ejemplo	(300 MHz, $CDCl_3$) δ 1.79 (m, 4H), 2.62 (m, 4H), 3.88 (s, 2H), 4.64 (br s, 2H), 5.40 (s, 2H), 7.21 (d, J = 2.3 Hz, 1H), 7.26 (m, 1H), 7.38 (m, 5H), 7.84 (s, 1H), 8.01 (d, J = 1.8 Hz, 1H), 8.10 (br s, 1H)	467
I- 64		3- (2,6- dicloro- benciloxi)- 5- (3- dietilaminometil- 1H- indol- 5- il)- piridin- 2- ilamina	3.23	Ver ejemplo	(300 MHz, $CDCl_3$) δ 1.13 (t, 6H), 2.64 (q, 4H), 3.88 (s, 2H), 4.66 (br s, 2H), 5.37 (s, 2H), 7.19 (d, J = 1.7 Hz, 1H), 7.26 (m, 1H), 7.37 (m, 5H), 7.86 (s, 1H), 8.00 (d, J = 1.7 Hz, 1H), 8.44 (br s, 1H)	469
I- 65		Terbutil ester del ácido (1- {5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 3- ilmetil}- (3R)- pirrolidin- 3- il)- carbamico	6.3	Ver ejemplo	(300 MHz, $CDCl_3$) δ 1.39 (s, 9H), 2.22 (m, 1H), 2.40 (m, 1H), 2.58 (m, 1H), 2.68 (m, 1H), 2.99 (m, 1H), 3.82 (d, 1H), 3.88 (d, 1H), 4.16 (m, 1H), 4.65 (br s, 2H), 4.81 (m, 1H), 5.41 (s, 2H), 7.17 (d, J = 2.1 Hz, 1H), 7.26 (m, 1H), 7.38 (m, 5H), 7.81 (s, 1H), 8.00 (d, J = 1.8 Hz, 1H), 8.09 (br s, 1H)	582
I- 66		3- (2,6- dicloro- benciloxi- - 5- [3- (2,6- dimetil- morfolin- 4- ilmetil)- 1H- indol- 5- il]- piridin- 2- ilamina	>20	Ver ejemplo	(300 MHz, $CDCl_3$) δ 1.13 (d, J = 6.3 Hz, 6H), 1.80 (t, J = 10.7 Hz, 2H), 1.94 (br s, 1H), 2.84 (d, J = 10.5 Hz, 2H), 3.72 (m, 4H), 4.68 (br s, 2H), 5.39 (s, 2H), 7.16 (d, J = 2.2 Hz, 1H), 7.26 (m, 1H), 7.38 (m, 5H), 7.89 (s, 1H), 8.10 (d, J = 1.7 Hz, 1H), 8.32 (br s, 1H)	511
I- 67		N- (1- {5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 3- ilmetil}- (3R)- pirrolidin- 3- il)- acetamida	1.79	Ver ejemplo	(300 MHz, $CDCl_3$) δ 1.86 (s, 3H), 2.31 (m, 2H), 2.59 (m, 1H), 2.70 (m, 1H), 2.99 (m, 1H), 3.82 (d, 1H), 3.90 (d, 1H), 4.42 (m, 1H), 4.68 (br s, 2H), 5.40 (s, 2H), 5.91 (m, 1H), 7.15 (d, J = 2.2 Hz, 1H), 7.26 (m, 2H), 7.38 (m, 5H), 7.82 (s, 1H), 8.00 (d, J = 1.8 Hz, 1H), 8.33 (br s, 1H)	524

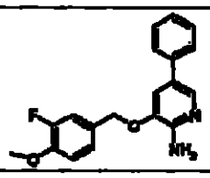
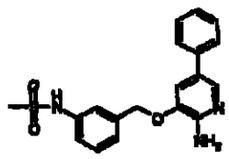
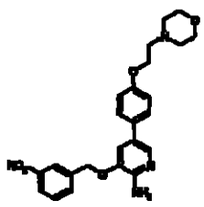
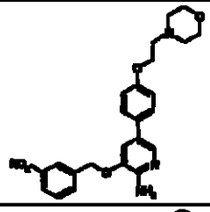
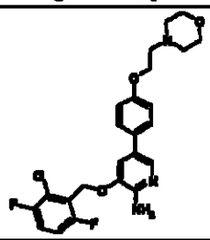
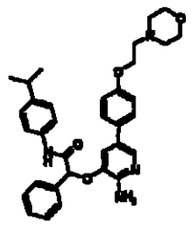
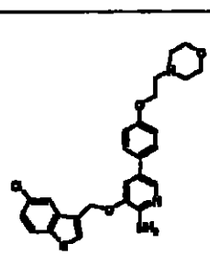
No.	Estructura	Nombre	Met IC_{20} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 68		1- (4- {5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 3- ilmetil}- piperazina- 1- il) etanona	2.18	Ver ejemplo	(300 MHz, $CDCl_3$) δ 2.07 (s, 3H), 2.51 (m, 4H), 3.44 (m, 2H), 3.63 (m, 2H), 3.78 (s, 2H), 4.68 (br s, 2H), 5.40 (s, 2H), 7.17 (d, J = 2.2 Hz, 1H), 7.26 (m, 1H), 7.38 (m, 5H), 7.88 (s, 1H), 8.00 (d, J = 1.8 Hz, 1H), 8.34 (br s, 1H)	524
I- 69		3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (1H- indol- 5- il)- piridin- 2- ilamina		Ver ejemplo		386
I- 70		1- (4- {5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- 1H- indol- 3- ilmetil}- piperazina- 1- il)etanona	0.8	Ver ejemplo	(300 MHz, $CDCl_3$) δ 2.08 (s, 3H), 2.49 (m, 4H), 3.48 (m, 2H), 3.61 (m, 2H), 3.80 (s, 2H), 4.68 (s, 2H), 5.30 (s, 2H), 7.02 (m, 1H), 7.20 (m, 2H), 7.41 (m, 3H), 7.89 (s, 1H), 8.06 (s, 1H), 8.63 (s, 1H)	526
I- 71		3- (2- cloro- 3,6- difluoro- benciloxi)- 5- [3(2,6- dimetil- morfolin- 4- ilmetil)- 1H- indol- 5- il]- piridin- 2- ilamina	2.71	Ver ejemplo	(300 MHz, $CDCl_3$) δ 1.37 (d, 6H), 1.92 (m, 2H), 2.95 (m, 2H), 3.87 (m, 4H), 4.68 (s, 2H), 5.34 (s, 2H), 7.08 (m, 1H), 7.27 (m, 2H), 7.48 (m, 3H), 7.89 (s, 1H), 7.98 (s, 1H), 8.21 (br s, 1H)	513
I- 72		N- (1- {5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- 1H- indol- 3- ilmetil}- (3S)- pirrolidin- 3- il)- acetamida	0.95	Ver ejemplo	(300 MHz, $CDCl_3$) δ 1.71 (m, 1H), 1.81(s, 3H), 2.31 (m, 2H), 2.48 (m, 1H), 2.79 (m, 2H), 3.11 (m, 1H), 3.98 (m, 2H), 4.68 (s, 2H), 5.31 (s, 2H), 7.06 (m, 1H), 7.20 (m, 2H), 7.45 (m, 4H), 7.86 (s, 1H), 7.98 (s, 1H), 8.38 (s, 1H)	526
I- 73		3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (3- piperidin- 1- ilmetil)- 1H- indol- 5- il)- piridin- 2- ilamina	0.74	Ver ejemplo	(300 MHz, $CDCl_3$) δ 1.84 (m, 2H), 1.64 (m, 4H), 2.56(m, 4H), 3.80 (s, 2H), 4.68 (s, 2H), 5.30 (s, 2H), 7.08 (m, 1H), 7.20 (m, 2H), 7.45 (m, 3H), 7.86 (s, 1H), 7.89 (s, 1H), 8.49 (br s, 1H)	483

No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^1H- NMR	MS m/z (M+1)
I- 74		3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (3- morfolin- 4- ilmetil- 1H- indol- 5- il)- piridin- 2- ilamina	1.4	Ver ejemplo	(300 MHz, $CDCl_3$) δ 2.72 (m, 4H), 3.80 (m, 6H), 4.70 (s, 2H), 5.33 (d, 2H), 7.07 (m, 1H), 7.20 (m, 1H), 7.35- 7.55 (m, 4H), 7.86 (s, 1H), 8.00 (d, 1H), 8.23 (s, 1H)	485
I- 75		3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (3- pirrolidin- 1- ilmetil- 1H- indol- 5- il)- piridin- 2- ilamina	0.7	Ver ejemplo	(300 MHz, $CDCl_3$) δ 1.86 (m, 4H), 2.79 (m, 4H), 4.01 (s, 2H), 4.63 (s, 2H), 5.30 (d, 2H), 7.05 (m, 1H), 7.18 (m, 1H), 7.30- 7.60 (m, 4H), 7.80 (s, 1H), 8.00 (d, 1H), 8.64 (s, 1H)	469
I- 76		Etil ester del acido 5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carboxilico	>20	Ver ejemplo	(400 MHz, DMSO- d_6) δ 1.34 (t, 3H), 4.34 (m, 2H), 5.34 (s, 2H), 5.58 (s, 2H), 7.16 (s, 1H), 7.52 (m, 2H), 7.84 (d, 2H), 11.84 (s, 1H)	456
I- 77		ácido 5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carboxílico	1.62	Ver ejemplo	(400 MHz, DMSO- d_6) δ 5.46 (s, 2H), 5.53 (s, 2H); 6.66 (s, 1H), 7.33 (d, 1H), 7.44 (m, 2H), 7.54 (m, 3H), 7.72 (s, 1H), 7.86 (s, 1H), 11.12 (s, 1H)	428
I- 78		{5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- il}- (4- metil- piperazin- 1- il)- metanona	0.18	Ver ejemplo	(400 MHz, DMSO- d_6) δ 2.21 (s, 3H), 2.36 (m, 4H), 3.74 (m, 4H), 5.35 (s, 2H), 5.53 (s, 2H), 6.78 (s, 1H), 7.50 (m, 6H), 7.81 (s, 1H), 7.88 (s, 1H), 11.56 (s, 1H)	510
I- 79		{5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- il}- [(3R)- 3- dimetilamino- pirrolidin- 1- il]- metanona	0.18	Ver ejemplo	(400 MHz, DMSO- d_6) δ 1.80 (m, 1H), 2.12 (m, 1H), 2.21 (s, 6H), 2.74 (m, 1H), 3.25 (m, 1H), 3.53 (m, 1H), 3.78 (m, 1H), 4.02 (m, 1H), 5.36 (s, 2H), 5.54 (s, 2H), 6.98 (s, 1H), 7.46 (m, 3H), 7.56 (m, 3H), 7.86 (m, 2H), 11.53 (s, 1H)	524

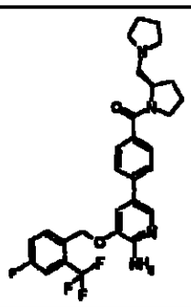
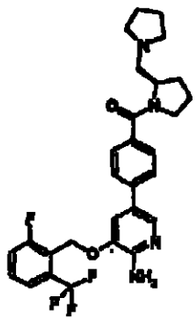
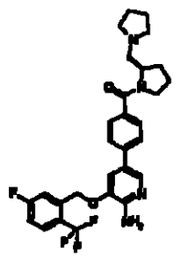
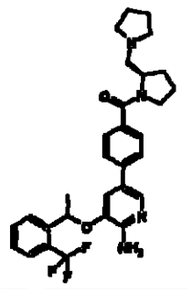
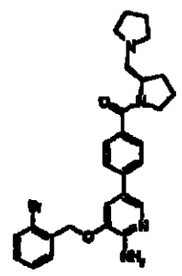
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 80		{5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- il}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	0.079	Ver ejemplo	(400 MHz, DMSO- d_6) δ 1.80 (m, 1H), 2.12 (m, 1H), 2.21 (a, 6H), 2.74 (m, 1H), 3.25 (m, 1H), 3.53 (m, 1H), 3.78 (m, 1H), 4.02 (m, 1H), 5.36 (s, 2H), 5.54 (s, 2H), 6.98 (s, 1H), 7.46 (m, 3H), 7.56 (m, 3H), 7.86 (m, 2H), 11.53 (s, 1H)	524
I- 81		ácido 5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carboxílico (2- pirrolidin- 1- il- etil)- amida	1.2	Ver ejemplo	(400 MHz, DMSO- d_6) δ 1.66 (m, 4H), 2.51 (m, 4H), 2.58 (t, 2H), 3.39 (m, 2H), 7.11 (s, 1H), 7.45 (m, 2H), 7.55 (m, 3H), 7.60 (m, 1H), 7.82 (s, 1H), 7.88 (s, 1H), 8.45 (t, 1H), 11.56 (s, 1H)	524
I- 82		ácido 5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carboxílico (2- morfolin- 4- il- etil)- amida	1.8	Ver ejemplo	(400 MHz, DMSO- d_6) δ 2.41 (m, 6H), 3.39 (m, 2H), 3.58 (m, 4H), 7.11 (s, 1H), 7.45 (m, 2H), 7.55 (m, 4H), 7.82 (s, 1H), 7.88 (s, 1H), 8.42 (t, 1H), 11.52 (s, 1H)	540
I- 83		Terbutil ester del ácido (1- {5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carbonil}- (3S)- pirrolidin- 3- il)- carbamico	5	Ver ejemplo	(400 MHz, DMSO- d_6) δ 1.38 (s, 9H), 1.64 (m, 1H), 1.98 (m, 2H), 3.18 (m, 2H), 3.78 (m, 2H), 5.37 (s, 2H), 5.53 (s, 2H), 6.92 (m, 1H), 7.26 (m, 1H), 7.48 (m, 2H), 7.56 (m, 3H), 7.61 (m, 1H), 7.86 (m, 2H), 11.52 (s, 1H)	596
I- 84		{5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- il}- [(3S)- 3- Amino- pirrolidin- 1- il]- metanona	0.14	Ver ejemplo	(400 MHz, DMSO- d_6) δ 2.20 (m, 2H), 2.68 (m, 1H), 3.84 (m, 4H), 5.56 (s, 2H), 7.52 (m, 6H), 7.94 (m, 5H), 8.62 (m, 2H)	496
I- 85		ácido 5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carboxílico (2- hidroxi- 3- pirrolidin- 1- il- propil)- amida	0.7	Ver ejemplo	(400 MHz, DMSO- d_6) δ 1.67 (m, 4H), 2.37 (m, 1H), 2.52 (m, 1H), 3.31 (m, 1H), 3.62 (m, 4H), 3.46 (m, 1H), 3.76 (m, 1H), 5.38 (s, 2H), 5.52 (s, 2H), 7.14 (s, 1H), 7.46 (m, 2H), 7.56 (m, 4H), 7.86 (m, 2H), 8.48 (t, 1H), 11.58 (s, 1H)	554
I- 86		4- (6- amino- 5- benciloxi- piridin- 3- il)- fenol	8.7	Ver ejemplo	(400 MHz, DMSO- d_6) δ 9.4 (s, 1H), 7.74 (d, J = 2 Hz, 1H), 7.52 (d, J = 7.2 Hz, 2H), 7.38 (m, 4H), 7.32 (m, 2H), 6.8 (d, J = 7.2 Hz, 2H), 5.69 (s, 2H), 5.22 (s, 2H)	293

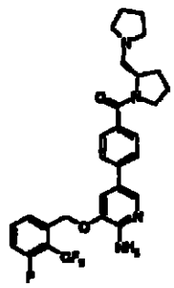
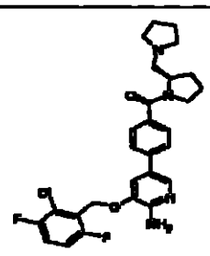
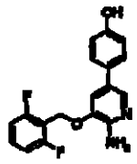
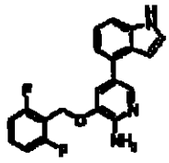
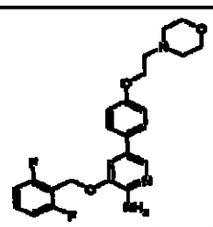
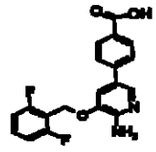
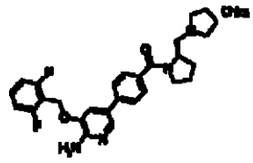
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 87		3- benciloxi- 5- fenil- piridin- 2- ilamina		Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.84 (d, 1H), 7.56 (d, 2H), 7.51 (d, 2H), 7.38 (m, 5H), 7.31 (t, 1H), 7.25 (t, 1H), 5.83 (br s, 2H), 5.24 (s, 2H)	277
I- 88		3- (3- metoxi- benciloxi)- 5- fenil- piridin- 2- ilamina		Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.85 (d, 1H), 7.56 (m, 2H), 7.38 (m, 3H), 7.28 (m, 2H), 7.08 (m, 2H), 6.86 (m, 1H), 5.84 (br s, 2H), 5.21 (s, 2H), 3.75 (s, 3H)	307
I- 89		3- (2- cloro- 4- fluoro- benciloxi)- 5- fenil- piridin- 2- ilamina	17	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.88 (s, 1H) 7.79 (m, 1H), 7.59 (m, 2H), 7.51 (dd, 1H), 7.40 (m, 3H), 7.27 (m, 2H), 5.84 (s, 2H), 5.24 (s, 2H)	329
I- 90		3- (2- cloro- benciloxi)- 5- fenil- piridin- 2- ilamina	48% a 20 uM	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.88 (d, 1H), 7.73 (m, 1H), 7.68 (m, 2H), 7.50 (m, 1H), 7.38 (m, 5H), 7.26 (m, 1H), 5.57 (s, 2H), 5.30 (s, 2H)	311
I- 91		3- (2,5- dicloro- benciloxi)- 5- fenil- piridin- 2- ilamina	48% a 20 uM	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.89 (d, 1H), 7.85 (d, 1H), 7.59 (m, 2H), 7.53 (d, 1H), 7.46 (d, 1H), 7.39 (m, 3H), 7.26 (m, 1H), 5.95 (s, 2H), 5.30 (s, 2H)	345
I- 92		3- (2- cloro- 5- trifluorometil- benciloxi)- 5- fenil- piridin- 2- ilamina	>20	Ver ejemplo	(400 MHz, DMSO- d_6) δ 8.16 (s, 1H), 7.89 (d, 1H), 7.76 (d, 2H), 7.59 (m, 2H), 7.48 (d, 1H), 7.39 (m, 2H), 7.26 (m, 1H), 5.90 (s, 2H), 5.36 (s, 2H)	379
I- 93		3- (2,4- dicloro- 5- fluoro- benciloxi)- 5- fenil- piridin- 2- ilamina	>20	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.95 (d, 1H), 7.88 (m, 2H), 7.60 (m, 2H), 7.44 (d, 1H), 7.39 (m, 2H), 7.26 (m, 1H), 6.01 (s, 2H), 5.24 (s, 2H)	364
I- 94		3- (2- cloro- 3- trifluorometil- benciloxi)- 5- fenil- piridin- 2- ilamina	>20	Ver ejemplo	(400 MHz, DMSO- d_6) δ 8.10 (d, 1H), 7.89 (d, 1H), 7.85 (m, 1H), 7.60 (m, 3H), 7.45 (d, 1H), 7.39 (m, 2H), 7.26 (m, 1H), 5.93 (s, 2H), 5.37 (s, 2H)	379

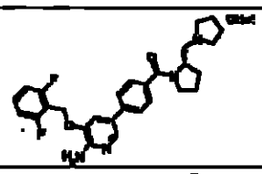
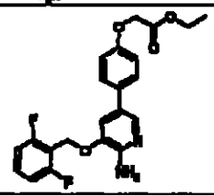
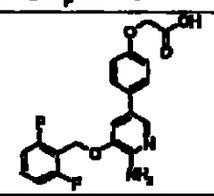
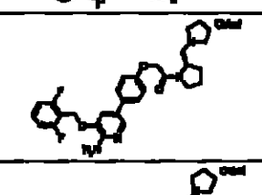
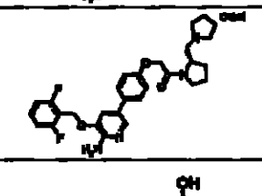
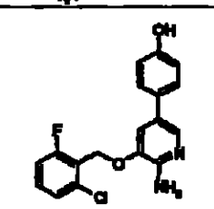
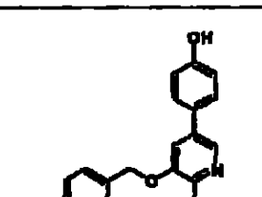
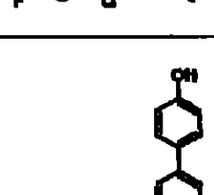
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 95		3- (2- cloro- 3,6- difluoro- benciloxi)- 5- fenil- piridin- 2- ilamina	0.64	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.89 (d, 1H), 7.57 (m, 4H), 7.40 (m, 3H), 7.26 (m, 1H), 5.72 (s, 2H), 5.28 (s, 2H)	347
I- 96		3- (3,4- dicloro- benciloxi)- 5- fenil- piridin- 2- ilamina	16.2	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.86 (d, 1H), 7.84 (d, 1H), 7.65 (m, 1H), 7.67 (m, 3H) 7.39 (m, 3H), 7.26 (m, 1H), 5.96 (s, 2H), 5.24 (s, 2H); MS m/z 345[M+1].	345
I- 97		2- (2- amino- 5- fenil- piridin- 3- iloximetil)- benzonitrilo	12.2	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.90 (dd, 2H), 7.82 (d, 1H), 7.75 (m, 1H), 7.56 (m, 3H), 7.48 (d, 1H), 7.40 (m, 2H), 7.26 (m, 1H), 5.85 (s, 2H), 5.39 (s, 2H)	302
I- 98		3- (2- cloro- 6- fluoro- 3- metil- benciloxi)- 5- fenil- piridin- 2- ilamina	7.6	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.88 (d, 1H), 7.61 (m, 2H), 7.53 (d, 1H), 7.43 (m, 3H), 7.25 (m, 2H), 5.65 (s, 2H), 5.27 (s, 2H), 2.34 (s, 3H)	342
I- 99		5- fenil- 3- (2,3,6- trifluoro- benciloxi)- piridin- 2- ilamina	3.9	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.89 (d, 1H), 7.61 (m, 3H), 7.52 (d, 1H), 7.40 (m, 2H), 7.25 (m, 2H), 5.75 (s, 2H), 5.26 (s, 2H)	331
I- 100		3- (2,6- difluoro- benciloxi)- 5- fenil- piridin- 2- ilamina	9.3	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.88 (d, 1H), 7.61 (m, 2H), 7.51 (m, 2H), 7.40 (m, 2H), 7.26 (m, 1H), 7.18 (m, 2H), 5.69 (s, 2H), 5.23 (s, 2h)	314
I- 101		3- (2,6- difluoro- 3- metil- benciloxi)- 5- fenil- piridin- 2- ilamina	12	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.88 (d, 1H), 7.60 (m, 2H), 7.51 (d, 1H), 7.40 (m, 3H), 7.27 (m, 1H), 7.07 (m, 1H), 5.68 (s, 2H), 6.21 (s, 2H)	328
I- 102		3- (3- cloro- 2,6- difluoro- benciloxi)- 5- fenil- piridin- 2- ilamina	9.6	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.88 (d, 1H), 7.74 (m, 1H), 7.61 (m, 2H), 7.51 (d, 1H), 7.40 (m, 2H), 7.27 (m, 2H), 5.76 (s, 2H), 5.26 (s, 2H)	347
I- 103		3- (2- cloro- 6- fluoro- benciloxi)- 5- fenil- piridin- 2- ilamina	7.91	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.88 (d, 1H), 7.61 (m, 2H), 7.52 (d, 1H), 7.49 (m, 1H), 7.40 (m, 3H), 7.30 (m, 2H), 5.67 (s, 2H), 5.27 (s, 2H)	329

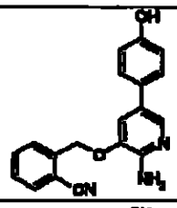
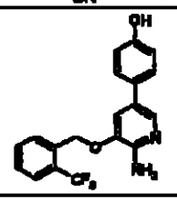
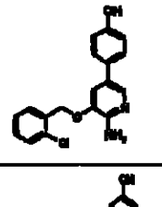
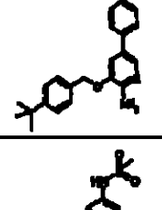
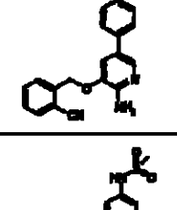
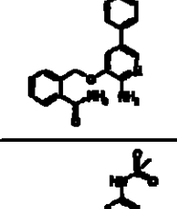
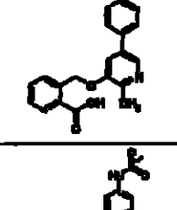
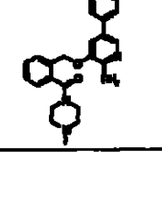
No.	Estructura	Nombre	Met IC_{20} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 104		3- (3- fluoro- 4- metoxi- benciloxi)- 5- fenil- piridin- 2- ilamina	15	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.84 (d, 1 H), 7.56 (m, 1H), 7.43 (d, 1H), 7.38 (m, 3H), 7.26 (m, 2H), 7.10 (m, 2H), 5.58 (s, 2H), 5.15 (s, 2H)	325
I- 105		N- [3- (2- amino- 5- fenil- piridin- 3- iloximetil)- fenil]- metanosulfonamida	>20	Ver ejemplo	(400 MHz, DMSO- d_6) δ 9.76 (s, 1H), 7.85 (d, J = 1.8 Hz, 1H), 7.57 (d, 2H), 7.38 (m, 5H), 7.28 (m, 2H), 7.15 (d, 1H), 5.85 (br s, 2H), 5.22 (s, 2H), 2.96 (s, 3H)	370
I- 106		5- [4- (2- morfolin- 4- il- etoxi)- fenil]- 3- (3- nitro- benciloxi)- piridin- 2- ilamina	12.6	Ver ejemplo	(DMSO- d_6) δ 2.50 (m, 4H), 2.69 (m, 2H), 3.57 (t, 4H), 4.09 (t, 2H), 5.37 (s, 2H), 5.85 (s, 2H), 6.96 (d, 2H), 7.38 (d, 1H), 7.48 (d, 2H), 7.69 (t, 1H), 7.81 (d, 1H), 8.01 (m, 1H), 8.17 (m, 1H), 8.36 (m,1H)	451
I- 107		5- [4- (2- morfolin- 4- il- etoxi)- fenil]- 3- (naftaleno- 1- ilmetoxi)- piridin- 2- ilamina	7.7	Ver ejemplo	(DMSO- d_6) δ 2.50 (m, 4H), 2.69 (t, 2H), 3.57 (t, 4H), 4.10 (t, 2H), 5.66 (s, 2H), 5.67 (s, 2H), 6.97 (d, 2H), 7.49- 7.61 (m, 5H), 7.78- 7.82 (m, 2H), 7.88- 7.98 (m, 2H), 8.20 (dd, 1H)	456
I- 108		3- (2- cloro- 3,6- difluoro- benciloxi)- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]piridin- 2- ilamina	0.21	Ver ejemplo	(400 MHz, $CDCl_3$) δ 2.60 (m, 4H), 2,83 (t, 2H), 3.74 (t, 4H), 4.16 (t, 2H), 4.63 (s, 2H), 5.27 (d, 2H), 6.98 (d, 2H), 7.02- 7.10 (m, 1H), 7.16- 7.22 (m, 1H), 7.30 (2, 2H), 7.44 (d, 2H), 7.91 (d, 1H)	476
I- 109		2- [2- amino- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 3- iloxi]- N- (4- isopropil- fenil)- 2- fenil- acetamida	>20	Ver ejemplo	(400 MHz, DMSO- d_6) δ 1.15 (d, 6H), 2.50 (m, 4H), 2.68 (m, 2H), 2.77- 2.89 (m, 1H), 3.57 (t, 6H), 4.08 (t, 2H), 6.15 (s, 1H), 6.20 (s, 2H), 6.93 (d, 2H), 7.17 (d, 1H), 7.30- 7.44 (m, 3H), 7.48 (d, 2H), 7.68 (d, 2H), 7.79 (d, 1H)	568
I- 110		3- (5- cloro- benzo[b]tiofen- 3- ilmetoxi)- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina	2.4	Ver ejemplo	(400 MHz, DMSO- d_6) δ 2.50 (m, 4H), 2.70 (m, 2H), 3.58 (t, 4H), 4.11 (t, 2H), 5.46 (s, 2H), 5.82 (s, 2H), 6.98 (d, 2H), 7.43 (dd, 1H), 7.50- 7.66 (m, 3H), 7.80 (d, 1H), 8.05 (d, 1H), 6.11 (d, 1H), 8.16 (s, 1H)	496.5

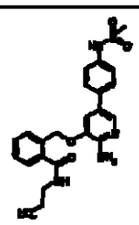
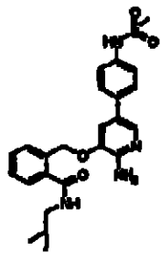
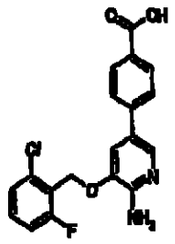
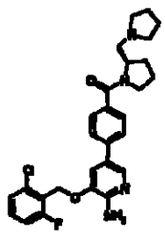
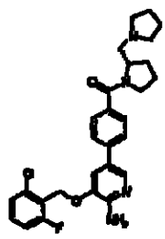
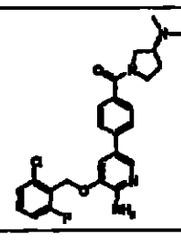
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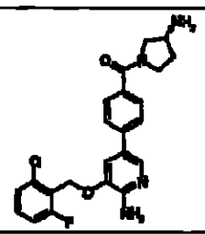
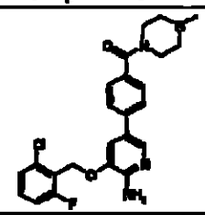
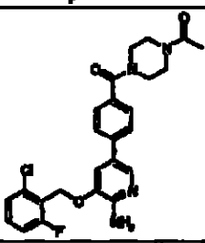
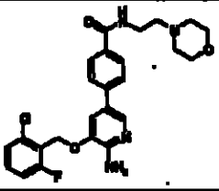
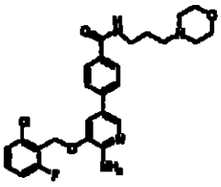
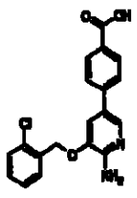
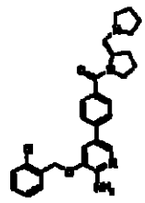
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 111		{4- [6- amino- 5- (4- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	1.51	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.94 (s, 2H), 7.71 (m, 4H), 7.44 (m, 3H), 5.92 (s, 2H), 5.36 (s, 2H), 4.21 (m, 1H), 3.52 (m, 2H), 2.69 (m, 5H), 1.96 (m, 2H), 1.84 (m, 3H), 1.66 (m, 4H)	543
I- 112		{4- [6- amino- 5- (2- fluoro- 6- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	0.15	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.94 (s, 1H), 7.69 (m, 3H), 7.59 (s, 1H), 7.50 (m, 2H), 5.72 (s, 2H), 5.26 (s, 2H), 4.16 (m, 1H), 3.47 (m, 2H), 2.63 (m, 5H), 1.96 (m, 2H), 1.86 (m, 3H), 1.68 (m, 4H)	543
I- 113		{4- [6- amino- 5- (5- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	1.27	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.95 (s, 1H), 7.85 (m, 2H), 7.63 (m, 2H), 7.48 (m, 2H), 7.42 (m, 2H), 6.04 (s, 2H), 5.36 (s, 2H), 4.16 (m, 1H), 3.44 (m, 2H), 2.62 (m, 5H), 1.96 (m, 2H), 1.85 (m, 3H), 1.66 (m, 4H)	543
I- 114		(4- {6- amino- 5- [1- (2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	0.33	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.85 (d, 1H), 7.81 (s, 1H), 7.76 (m, 2H), 7.41 (m, 5H), 7.03 (s, 1H), 6.16 (s, 2H), 5.81 (m, 1H), 4.10 (m, 1H), 3.41 (m, 2H), 2.59 (m, 5H), 1.94 (m, 2H), 1.82 (m, 3H) 1.64 (d, 3H), 1.48 (m, 4H)	539
I- 115		{4- [6- amino- 5- (2- bromo- benciloxi)- piridin- 3- il]- fenil}- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	1.75	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.74 (s, 1H), 7.68 (m, 3H), 7.45 (m, 5H), 7.31 (m, 1H), 5.92 (s, 2H), 5.25 (s, 2H), 4.16 (m, 1H), 3.43 (m, 2H), 2.62 (m, 5H), 1.94 (m, 2H), 1.82 (m, 3H), 1.65 (m, 4H)	537

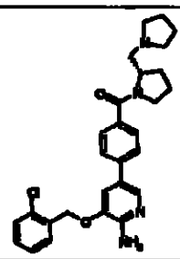
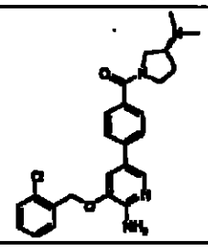
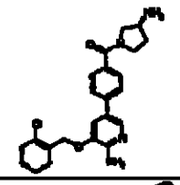
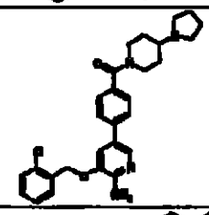
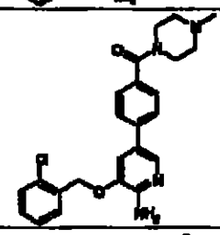
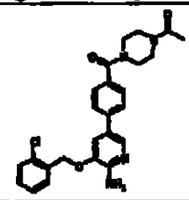
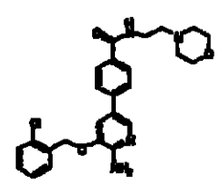
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 116		{4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	0.025	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.92 (s, 1 H), 7.66 (m, 4H), 7.46 (m, 4H), 5.89 (s, 2H), 6.39 (s, 2H), 4.19 (m, 1H), 3.50 (m, 2H), 2.54 (m, 5H), 1.95 (m, 2H), 1.83 (m, 3H), 1.64 (m, 4H)	543
I- 117		{4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	0.063	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.95 (d, 1H), 7.69 (d, 2H), 7.58 (m, 2H), 7.50 (d, 2H), 7.40 (m, 1H), 5.81 (s, 2H), 5.29 (s, 2H), 4.35 (m, 1H), 3.5 (d, 2H), 2.87 (d, 2H), 2.71 (d, 2H), 1.7- 2.0 (m, 10H)	527
I- 118		4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenol	3.79	Ver ejemplo	(400 MHz, DMSO- d_6) δ 9.38 (s, 1H), 7.77 (d, J = 2Hz 1H), 7.52 (m, 2H), 7.40 (m, 3H), 7.17 (m, 2H), 6.79 (m, 2H), 5.53 (br. s, 2H), 5.20 (s, 2H)	329
I- 119		3- (2,6- difluoro- benciloxi)- 5- (1H- indol- 4- il)- piridin- 2- ilamina	5.8	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.81 (d, J = 2Hz, 1H), 7.51 (m, 3H), 7.45 (d, J = 2Hz, 1H), 7.17 (m, 2H), 6.98 (m, 2H), 5.58 (s, 2H), 5.21 (s, 2H), 4.10 (t, 2H), 3.57 (t, 4H), 2.69 (t, 2H), 2.48 (t, 4H)	442
I- 120		3- (2,6- difluoro- benciloxi)- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina		Ver ejemplo	(400 MHz, DMSO- d_6) δ 11.18 (s, 1H), 7.86 (d, J = 2Hz, 1H), 7.52 (m, 1H), 7.44 (d, J = 2Hz, 1H), 7.36 (dd, 1H), 7.34 (m, 1H), 7.18 (m, 2H), 7.13 (dd, 1H), 7.02 (dd, 1H), 6.49 (m, 1H), 5.66 (s, 2H), 5.22 (s, 2H)	352
I-.121		ácido 4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- benzoico		Ver ejemplo	(400 MHz, DMSO- d_6) δ 12.85 (s, 1H), 7.94 (d, J = 2Hz, 1H), 7.89 (dd, 2H), 7.71 (dd, 2H), 7.55 (d, J = 2Hz, 1H), 7.47 (m, 1H), 7.13 (m, 2H), 5.83 (s, 2H), 5.19 (s, 2H)	357
I- 122		{4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	1.21	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.94 (d, 1H), 7.68 (dd, 2H), 7.56 (m, 1H), 7.51 (m, 3H), 7.18 (m, 2H), 5.79 (s, 2H), 5.29 (s, 2H), 3.48 (m, 1H), 2.65 (m, 4H), 2.48 (d, 2H), 1.86 (m, 10H)	493

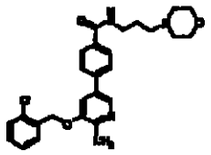
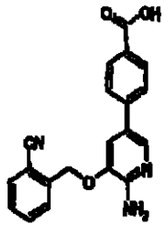
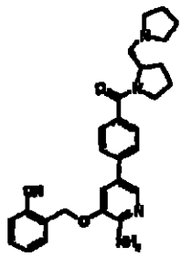
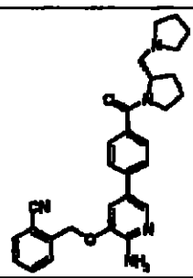
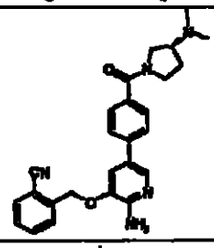
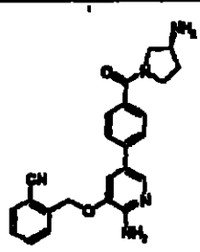
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 123		{4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	1.36	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.94 (d, 1H), 7.68 (dd, 2H), 7.56 (m, 1H), 7.51 (m, 3H), 7.18 (m, 2H), 5.78 (s, 2H), 5.24 (s, 2H), 4.6 (m, 1H), 3.5 (m, 2H), 2.52 (d, 4H), 1.86 (m, 10H)	493
I- 124		Etil ester del acido{4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenoxi}- acetico		Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.81 (d, J = 2Hz, 1H), 7.52 (m, 3H), 7.18 (m, 1H), 6.96 (m, 2H), 5.70 (br. s, 2H), 5.23 (s, 2H), 4.79 (s, 2H), 2.68 (q, 4H), 1.21 (t, 3H)	415
I- 125		Acido {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenoxi}- acetico	14.7	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.79 (d, 1H), 7.51 (m, 1H), 7.47 (m, 1H), 7.44 (m, 2H), 7.17 (m, 2H), 7.05 (m, 2H), 5.55 (br. s, 2H), 5.21 (s, 2H), 4.25 (s, 2H)	387
I- 126		2- {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenoxi}- 1- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- etanona	3.58	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.81 (d, 1H), 7.51 (m, 3H), 7.45 (d, 1H), 7.18 (m, 2H), 6.80 (m, 2H), 5.65 (s, 2H), 5.22 (s, 2H). 4.80 (dd, 2H), 4.29 (m, 1H), 3.53 (m, 2H), 3.20 (m, 4H), 1.93 (m, 10H)	523
I- 127		2- {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenoxi}- 1- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- etanona	5.43	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.81 (d, 1H), 7.52 (m, 3H), 7.46 (d, 1H), 7.18 (m, 2H), 7.00 (m, 2H), 5.66 (s, 2H), 5.22 (s, 2H), 4.80 (dd, 2H), 4.60 (m, 1H), 3.53 (m, 2H), 3.19 (m, 4H), 1.96 (m, 10H)	523
I- 128		4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenol	3.99	Ver ejemplo	(400 MHz, DMSO- d_6) δ 9.38 (s, 1H), 7.77 (d, 1H), 7.50 (m, 1H), 7.42 (m, 4H), 7.39 (m, 1H), 6.80 (m, 2H), 5.50 (s, 2H), 5.24 (s, 2H)	345
I- 129		4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- fenol	19	Ver ejemplo	(DMSO- d_6) δ 5.21 (s, 2H), 5.67 (s, 2H), 6.80 (d, 2H), 7.26 (t, 1H), 7.34 (s, 1H), 7.41 (d, 2H), 7.50 (d, 1H), 7.79 (m, 2H), 9.38 (s, 1H)	345
I- 130		4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- fenol	9/>20	Ver ejemplo	(DMSO- d_6) δ 5.21 (s, 2H), 5.71 (s, 2H), 6.81 (d, 2H), 7.40 (m, 5H), 7.74 (m, 2H), 9.38 (s, 1H)	361

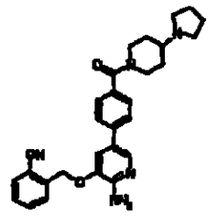
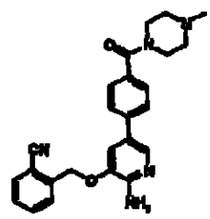
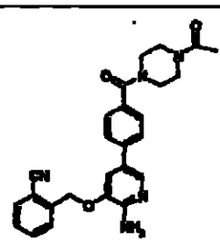
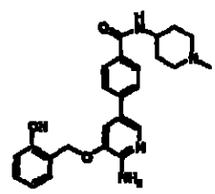
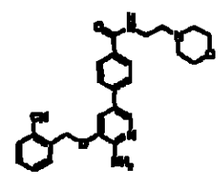
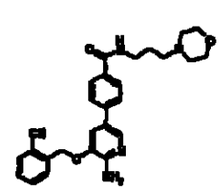
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 131		2- [2- amino- 5- (4- hidroxi- fenil)- piridin- 3- iloximetil]- benzonitrilo	19	Ver ejemplo	(DMSO- d_6) δ 5.35 (s, 2H), 5.68 (s, 2H), 6.77 (d, 2H), 7.41 (m, 3H), 7.54 (t, 1H), 7.78 (m, 3H), 7.92 (d, 1H), 9.38 (s, 1H)	318
I- 132		4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenol	3.67	Ver ejemplo	(400 MHz, DMSO- d_6) δ 5.32 (s, 2H), 5.68 (s, 2H), 6.78 (d, 2H), 7.26 (s, 1H), 7.36 (d, 2H), 7.57 (t, 1H), 7.72 (t, 1H), 7.78 (m, 2H), 7.86 (m, 1H), 9.38 (s, 1H)	361
I- 133		4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenol	13.8	Ver ejemplo	(DMSO- d_6) δ 5.25 (s, 2H), 5.69 (s, 2H), 6.78 (d, 2H), 7.38 (m, 5H), 7.50 (m, 1H), 7.71 (m, 1H), 7.78 (s, 1H), 9.38 (s, 1H)	326
I- 134		4- [6- amino- 5- (4- *terc*- butil- benciloxi)- piridin- 3- il]- fenol	4	Ver ejemplo	(DMSO- d_6) δ 1.26 (s, 9H), 5.16 (s, 2H), 5.63 (s, 2H), 6.78 (d, 2H), 7.40 (m, 7H), 7.72 (s, 1H), 9.36 (s, 1H)	349
I- 135		N- {4- [6- amino- 5- (2- ciano- benciloxi)- piridin- 3- il]- fenil} metanosulfonamida	4.18	Ver ejemplo	(DMSO- d_6) δ 2.98 (s, 3H), 5.36 (s, 2H), 5.82 (s, 2H), 7.24 (d, 2H), 7.42 (s, 1H), 7.58 (m, 3H), 7.75 (t, 1H), 7.89 (m, 3H), 9.70 (s, 1H)	393
I- 136		2- [2- amino- 5- (4- metanosulfonilamino- fenil)- piridin- 3- iloximetil]- benzamida	>20	Ver ejemplo	(DMSO- d_6) δ 2.88 (s, 3H), 5.37 (s, 2H), 5.75 (s, 2H), 7.15 (d, 2H), 7.30 (s, 1H), 7.48 (m, 6H), 7.20 (d, 1H), 7.80 (s, 1H), 7.90 (s, 1H)	413
I- 137		Ácido 2- [2- amino- 5- (4- metanosulfonilamino- fenil)- piridin- 3- iloximetil]- benzoico	>20	Ver ejemplo	(DMSO- d_6) δ 3.00 (s, 3H), 5.65 (s, 2H), 7.26 (d, 2H), 7.47 (m, 3H), 7.60 (m, 4H), 7.72 (m, 1H), 7.82 (s, 1H), 7.94 (d, 1H), 9.84 (s, 1H)	414
I- 138		N- (4- {6- amino- 5- [2- (4- metil- piperazina- 1- carbonil)- benciloxi]- piridin- 3- il}- fenil) metanosulfonamida	>20	Ver ejemplo	(DMSO- d_6) δ 2.08 (s, 3H), 2.26 (m, 2H), 2.96 (s, 3H), 3.15 (m, 2H), 3.36 (m, 2H), 3.59 (m, 2H), 5.17 (br s, 2H), 5.78 (s, 2H), 7.23 (d, 2H), 7.28 (m, 1H), 7.36 (s, 1H), 7.43 (m, 2H), 7.57 (m, 4H), 7.84 (s, 1H)	496

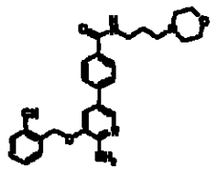
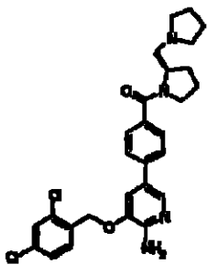
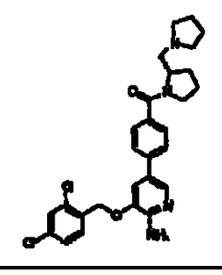
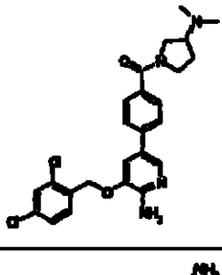
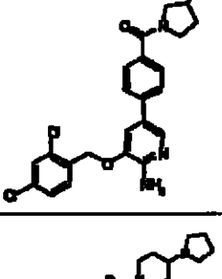
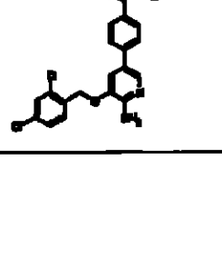
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 139		2- [2- amino- 5- (4- metanosulfonilamino- fenil)- piridin- 3- iloximetil]- N- (2- hidroxi- etil)- benzamida	>20	Ver ejemplo	(DMSO- d_6) δ 2.96 (s, 3H), 3.28 (m, 2H), 3.46 (m, 2H), 4.70 (s, 1H), 5.30 (s, 2H), 5.78 (s, 2H), 7.23 (d, 2H), 7.32 (s, 1H), 7.39 (m, 1H), 7.47 (m, 2H), 7.53 (m, 2H), 7.62 (d, 1H), 7.83 (s, 1H), 8.37 (t, 1H), 9.72 (br s, 1H)	457
I- 140		2- [2- amino- 5- (4- metanosulfonilamino- fenil)- piridin- 3- iloximetil]- N- isobutil- benzamida	>20	Ver ejemplo	(DMSO- d_6) δ 0.84 (d, 6H), 1.78 (m, 1H), 2.82 (s, 3H), 3.03 (t, 2H), 5.28 (s, 2H), 5.72 (s, 2H), 7.12 (d, 2H), 7.24 (s, 1H), 7.42 (m, 5H), 7.62 (d, 1H), 7.79 (s, 1H), 8.41 (t, 1H), 9.68 (s, 1H)	469
I- 141		ácido 4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- benzoico		Ver ejemplo	(400 MHz, DMSO- d_6) δ 5.25 (s, 2H, CH_2), 5.82 (br s, 2H, NH_2), 6.30 - 8.00 (multiples, 9H, aromaticos)	373
I- 142		[4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	0.63	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, 1H), 7.57 (m, 4H), 7.10 (m, 3H), 7.04 (t, 1H), 5.30 (s, 2H), 4.83 (s, 2H), 4.45.(m, 1H), 3.40 (m, 2H), 2.90 (m, 4H), 2.2- 1.5 (m, 10H)	509
I- 143		{4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	13	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, 1H), 7.57 (m, 4H), 7.10 (m, 3H), 7.04 (t, 1H), 5.30 (s, 2H), 4.83 (s, 2H), 4.45 (m, 1H), 3.40 (m, 2H), 2.90 (m, 4H), 2.2- 1.5 (m, 10H)	509
I- 144		{4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona	1.7	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.58 (m, 4H), 7.36 (m, 3H), 7.05 (t, 1H), 5.30 (s, 2H), 5.07 (s, 2H), 3.9 (m, 1H), 3.6 (m, 2H), 3.4 (m, 1H), 3.0 (m, 1H), 2.37 (s, 3H), 2.27 (s, 3H), 1.8 (m, 2H)	470

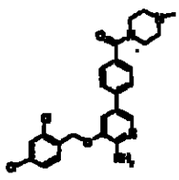
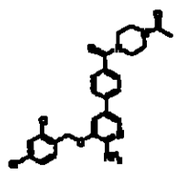
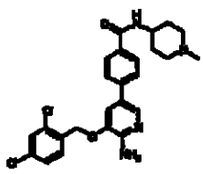
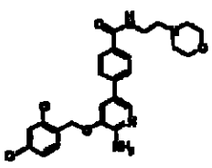
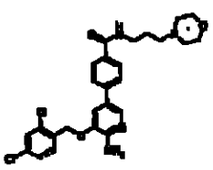
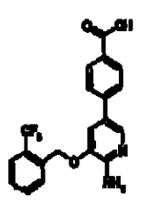
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 145		{4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il]- metanona	0.63	Ver ejemplo		441
I- 146		{4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona	1.94	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.93 (d, J = 1.7 Hz, 1H), 7.56 (d, J = 8.1 Hz, 2H), 7.48 (d, J = 8.1 Hz, 2H), 7.28 (m, 3H), 7.07 (t, J = 8.8 Hz), 5.30 (s, 2H), 5.05 (br s, 2H), 3.75 (m, 4H), 2.48 (m, 4H), 2.34 (s, 3H)	455
I- 147		1- (4- {4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- benzoil}- piperazin- 1- il]- etanona	1.45	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.91 (d, J = 1.7 Hz, 1H), 7.58 (d, J = 8.2 Hz, 2H), 7.50 (d, J = 8.2 Hz, 2H), 7.35 (m, 3H), 7.08 (t, J = 8.2 Hz), 5.32 (br s, 2H), 3.60 (m, 8H), 2.14 (s, 3H)	484
I- 148		4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida	6.4	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.7 Hz, 1H), 7.85 (d, J = 8.2 Hz, 2H), 7.65 (d, J = 8.2 Hz, 2H), 7.30 (m, 2H), 7.24 (d, J = 1.7 Hz, 1H), 7.08 (m, 1H), 6.95 (br t, 1H), 5.32 (s, 2H), 5.06 (br s, 2H), 3.82 (m, 4H), 3.64 (m, 2H), 2.76 (m, 2H), 2.65 (m, 4H)	485
I- 149		4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- il- propil)- benzamida	5.6	Ver ejemplo	(300 MHz, $CDCl_3$) δ 8.02 (br t, 1H), 7.95 (d, J = 1.7 Hz, 1H), 7.90 (d, J = 8.3 Hz, 2H), 7.59 (d, J = 8.3 Hz, 2H), 7.39 (d, J = 1.7 Hz, 1H), 7.30 (m, 2H), 7.08 (m, 1H), 6.95 (br t, 1H), 5.32 (s, 2H), 5.10 (br s, 2H), 3.78 (m, 4H), 3.62 (m, 2H), 2.64 (m, 6H), 1.87(m, 2H)	499
I- 150		ácido 4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- benzoico		Ver ejemplo	(400 MHz, DMSO- d_6) δ 5.30 (s, 2H, CH_2), 5.95 (br s, 2H, NH_2), 7.35 - 7.95 (multiples, 10H, aromaticos).	353 (M- 1)
I- 151		{4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenil}- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	0.87	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.6 Hz, 1H), 7.52 (m, 6H), 7.25 (m, 2H), 7.21(d, J = 1.6 Hz, 1H), 5.26 (s, 2H), 4.88 (br s, 2H), 4.32 (m, 1H), 3.52 (m, 2H), 2.89 (m, 4H), 2.2- 1.5 (m, 10H).	491

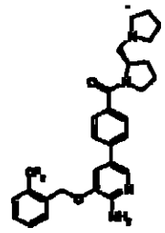
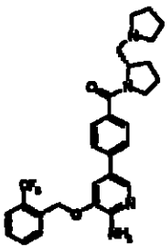
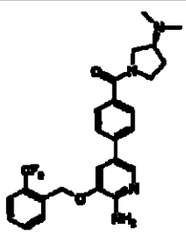
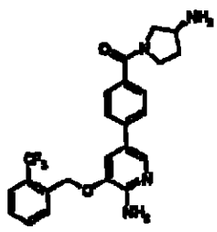
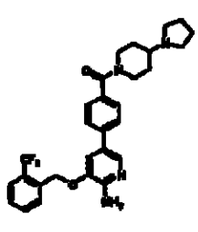
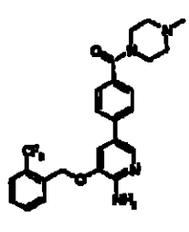
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 152		{4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	2.3	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.6 Hz, 1H), 7.52 (m, 6H), 7.25 (m, 2H), 7.21(d, J = 1.6 Hz, 1H), 5.26 (s, 2H), 4.88 (br s, 2H), 4.32 (m, 1H), 3.52 (m, 2H), 2.89 (m, 4H), 2.2- 1.5 (m, 10H). MS m/z 491[M+1]	491
I- 153		{4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona	12.7	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.53 (m, 6H), 7.33 (m, 2H), 7.27 (s, 1H), 5.26 (s, 2H), 4.94 (br s, 2H), 3.90 (m, 1H), 3.60 (m, 2H), 3.45 (m, 1H), 2.85 (m, 1H), 2.32 (s, 3H), 2.23 (s, 3H), 1.89 (m, 2H)	451
I- 154		{4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il]- metanona	1.44	Ver ejemplo		423
I- 155		{4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	1.5	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.8 Hz, 1H), 7.47 (m, 6H), 7.32 (m, 2H), 7.21 (d, J = 1.8 Hz, 1H), 5.26 (s, 2H), 4.86 (br s, 2H), 3.95 (m, 4H), 2.55 (m, 4H), 2.30 (m, 1H), 1.95 (m, 2H), 1.76 (m, 4H), 1.52 (m, 2H).	491
I- 156		{4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona	2.1	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.94 (d, J = 1.8 Hz, 1H), 7.49 (m, 6H), 7.32 (m, 2H), 7.21 (d, J = 1.8 Hz, 1H), 5.27 (s, 2H), 4.00 (br s, 2H), 3.80 (m, 4H), 2.50 (m, 4H), 2.35 (s, 3H)	437
I- 157		1- (4- {4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- benzoil}- piperazin- 1- il)- etanona	3.8	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.95 (d, J = 1.8 Hz, 1H), 7.51 (m, 6H), 7.33 (m, 2H), 7.21 (d, J = 1.8 Hz, 1H), 5.27 (s, 2H), 4.94 (br s, 2H), 3.65 (m, 8H), 2.14 (s, 3H)	465
I- 158		4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- N- (2 morfolin- 4- il- etil)- benzamida	8.9	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.95 (d, J = 1.8 Hz, 1H), 7.84 (d, J = 8.3 Hz, 2H), 7.55 (d, J = 8.3 Hz, 2H), 7.51 (m, 1H), 7.43 (m, 1H), 7.34 (me, 2H), 7.24 (d, J = 1.8 Hz, 1H), 7.01 (br t, 1H), 5.27 (d, 2H), 5.18 (br s, 2H), 3.77 (m, 4H), 3.61 (m, 2H), 3.25 (m, 2H), 2.70 (m, 2H), 2.60 (m, 4H)	467

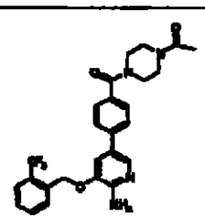
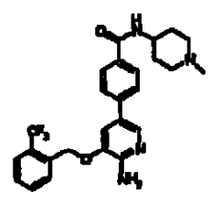
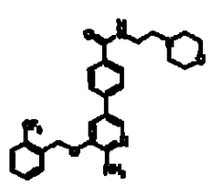
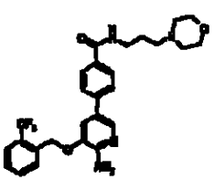
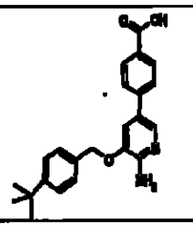
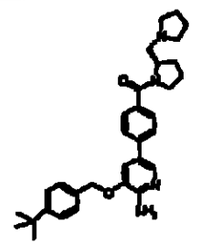
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 159		4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- N- (3 morfolin- 4- il- propil)- benzamida	4.5	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.95 (d, J = 1.8 Hz, 1H), 7.84 (d, J = 8.3 Hz, 2H), 7.55 (d, J = 8.3 Hz, 2H), 7.51 (m, 2H), 7.43 (m, 1H), 7.34 (m, 2H), 7.24 (d, J = 1.8 Hz, 1H), 5.27 (s, 2H), 4.97 (br s, 2H), 3.75 (m, 4H), 3.59 (m, 2H), 3.25 (m, 2H), 2.57 (m, 4H), 1.83 (m, 2H).	481
I- 160		ácido 4- [6- amino- 5- (2- ciano- benciloxi)- piridin- 3- il]- benzoico		Ver ejemplo	(400 MHz, DMSO- d_6) δ 5.35 (s, 2H, CH_2), 5.95 (br s, 2H, NH_2), 7.50- 8.00 (multiples, 10H, Aromaticos)	346
I- 161		2- {2- amino- 5- [4- ((2H)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carbonil)- fenil]- piridin- 3- iloximetil}- benzonitrilo	1.2	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.99 (d, J = 1.6 Hz, 1H), 7.76 (d, J = 7.5 Hz, 2H), 7.50 (m, 6H), 7.24 (d, J = 1.6 Hz, 1H), 5.35 (s, 2H), 4.88 (br s, 2H), 4.46 (m, 1H), 3.52 (m, 2H), 3.24 (m, 4H), 2.2- 1.5 (m, 10H)	482
I- 162		2- {2- amino- 5- [4- ((2S)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carbonil)- fenil]- piridin- 3- iloximetil}- benzonitrilo	2	Ver ejemplo	^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (d, J = 1.6 Hz, 1H), 7.76 (d, J = 7.5 Hz, 2H), 7.50 (m, 6H), 7.24 (d, J = 1.6 Hz, 1H), 5.35 (s, 2H), 4.88 (br s, 2H), 4.46 (m, 1H), 3.52 (m, 2H), 3.24 (m, 4H), 2.2- 1.5 (m, 10H).	482
I- 163		2- {2- amino- 5- [4- ((3S)- 3- dimetilamino- pirrolidina- 1- carbonil)- fenil]- piridin- 3- iloximetil}- benzonitrilo	>20	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.76 (d, J = 7.6 Hz, 2H), 7.50 (m, 6H), 7.26 (s, 1H), 5.36 (s, 2H), 4.99 (br s, 2H), 3.90 (m, 1H), 3.60 (m, 2H), 3.45 (m, 1H), 2.85 (m, 1H), 2.32 (s, 3H), 2.23 (s, 3H), 1.89 (m, 2H)	442
I- 164		2- {2- amino- 5- [4- ((3S)- 3- amino- pirrolidina- 1- carbonil)- fenil]- piridin- 3- iloximetil}- benzonitrilo	2.05	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.98 (d, J = 1.4 Hz., 1H), 7.76 (d, J = 7.5 Hz, 2H), 7.50 (m, 6H), 7.24 (d, J = 1.4 Hz, 1H), 5.35 (s, 2H), 4.91 (br s, 2H), 3.70 (m, 4H), 2.15 (m, 1H), 2.23 (s, 2H), 1.25 (m, 1H), 1.05(m,1H)	414

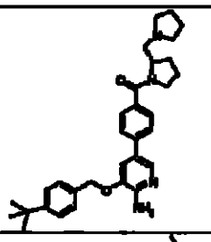
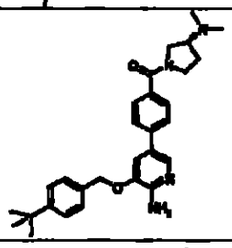
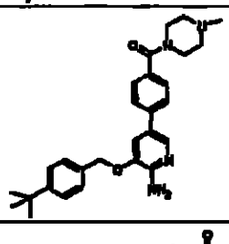
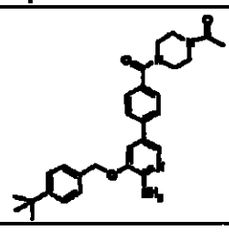
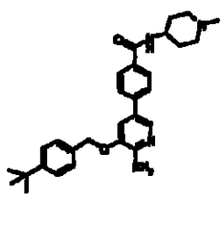
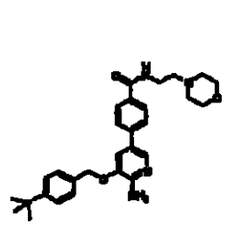
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 165		2- {2- amino- 5- [4- (4- pirrolidin- 1- il- piperidina- 1- carbonil)- fenil]- piridin- 3- iloximetil}- benzonitrilo	3.9	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.97 (d, J = 1.7 Hz,, 1H), 7.76 (d, J = 7.5 Hz, 2H), 7.66 (m, 2H), 7.51 (m,2H), 7.46 (m, 2H), 7.23 (d, J= 1.4 Hz, 1H), 5.35 (s, 2H), 4.88 (br s, 2H), 3.95 (m, 4H), 2.55 (m, 4H), 2.30 (m, 1H), 1.95 (m, 2H), 1.76 (m, 4H), 1.52 (m, 2H)	482
I- 166		2- [2- amino- 5- [4- (4- metil- piperazina- 1- carbonil)- fenil]- piridin- 3- iloximetil]- benzonitrilo	3.2	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.8 Hz,, 1H), 7.76 (d, J = 7.5 Hz, 2H), 7.66 (m, 2H), 7.51 (m,2H), 7.48 (m, 2H), 7.24 (d, J = 1.4 Hz, 1H), 5.35 (s, 2H), 5.01 (br s, 2H), 3.65 (m, 4H), 2.45 (m, 4H), 2.36 (s, 3H)	428
I- 167		2- {5- [4- (4- acetil- piperazina- 1- carbonil)- fenil]- 2- amino- piridin- 3- iloximetil}- benzonitrilo	5.7	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.95 (d, J = 1.7 Hz,, 1H), 7.76 (d, J = 7.5 Hz, 2H), 7.66 (m, 2H), 7.54 (m,2H), 7.50 (m, 2H), 7.26 (d, J = 1.4 Hz, 1H), 5.36 (s, 2H), 5.27 (br s, 2H), 3.65 (m, 8H), 2.14 (s, 3H)	456
I- 168		4- [6- amino- 5- (2- ciano- benciloxi)- piridin- 3- il]- N- (1- metil- piperidin- 4- il)- benzamida	10.8	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.99 (d, J = 1.8 Hz,, 1H), 7.82 (d, J = 8.3 Hz, 2H), 7.74 (m, 1H), 7.66 (m,2H), 7.55 (m, 3H), 7.25 (d, J = 1.8 Hz, 1H), 6.18 (d, J = 8.0 Hz, 1H), 5.35 (s, 2H), 4.88 (br s, 2H), 4.05 (m, 1H), 2.96 (m, 1H), 2.46 (s, 3H), 2.40 (m, 1H), 2.05 (m, 1H), 1.79 (m, 1H), 1.65 (m, 2H), 0.95 (m, 2H)	442
I- 169		4- [6- amino- 5- (2- ciano- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida	8.6	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.98 (d, J = 1.8 Hz,, 1H), 7.85 (d, J = 8.4 Hz, 2H), 7.76 (d, J =7.4 Hz, 1H), 7.66 (m, 2H), 7.57 (m, 3H), 7.27 (d, J = 1.8 Hz, 1H), 7.06 (m, 1H), 5.36 (s, 2H), 5.14 (br s, 2H), 3.78 (m, 4H), 3.63 (m, 2H), 2.73 (m, 2H), 2.63 (m, 4H)	458
I- 170		4- [6- amino- 5- (2- ciano- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- il- propil)- benzamida	17.3	Ver ejemplo	(300 MHz, $CDCl_3$) δ 8.01 (d, J = 1.7 Hz, 1H), 7.87 (d, J = 8.4 Hz, 2H), 7.76 (d, J = 7.5 Hz, 1H), 7.67 (m, 1H), 7.56 (d, J = 8.4Hz,2H), 7.45 (m, 3H), 7.27 (d, J = 1.8 Hz, 1H), 5.36 (s, 2H), 4.89 (br s, 2H), 3.74 (m, 4H), 3.60 (m, 2H), 2.57 (m, 6H), 1.82 (m, 2H)	472

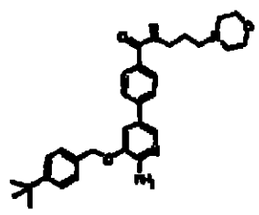
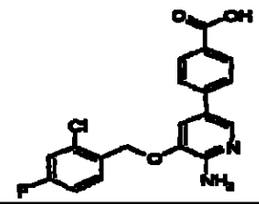
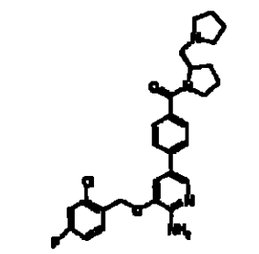
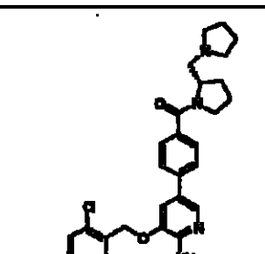
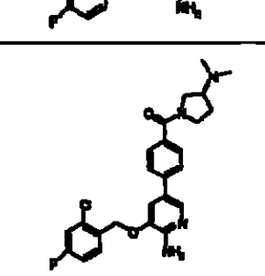
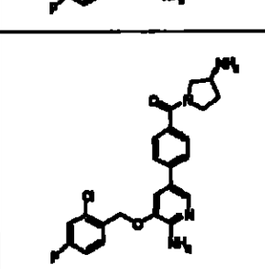
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 171		ácido 4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- benzoico		Ver ejemplo	(400 MHz, DMSO- d_6) δ 5.35 (s, 2H, CH_2), 5.90 (br s, 2H, NH_2), 7.30- 8.00 (multiples, 9H, Aromaticos)	389
I- 172		[4- [6- amino- 5- (2,4- diclorobenciloxi)- piridin- 3- il]- fenil)- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	0.61	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.97 (d, J = 1.7 Hz, 1 H), 7.47 (m, 6H), 7.30 (dd, J = 2.0 Hz, J = 8.3 Hz, 1H), 7.18 (d, J = 1.7 Hz, 1H), 5.21 (s, 2H), 4.85 (br s, 2H), 4.42 (m, 1H), 3.50 (m, 2H), 2.84 (m, 4H), 2.2- 1.5 (m, 10H)	527
I- 173		[4- [6- amino- 5- (2,4- diclorobenciloxi)- piridin- 3- il]- fenil)- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	0.66	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.97 (d, J = 1.7 Hz, 1H), 7.47 (m, 6H), 7.30 (dd, J = 2.0 Hz, J = 8.3 Hz, 1H), 7.18 (d, J = 1.7 Hz, 1H), 5.21 (s, 2H), 4.85 (br s, 2H), 4.42 (m, 1H), 3.50 (m, 2H), 2.84 (m, 4H), 2.2- 1.5 (m, 10H)	527
I- 174		[4- [6- amino- 5- (2,4- diclorobenciloxi)- piridin- 3- il]- fenil)- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona	0.8	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.50 (m, 6H), 7.30 (dd, J = 1.9 Hz, J = 8.3 Hz, 1H), 7.20 (s, 1H), 5.21 (s, 2H), 5.07 (br s, 2H), 3.90 (m, 1H), 3.62 (m, 2H), 3.45 (m, 1H), 2.85 (m, 1H), 2.32 (s, 3H), 2.23 (s, 3H), 1.89 (m, 2H)	486
I- 175		[4- [6- amino- 5- (2,4- diclorobenciloxi)- piridin- 3- il]- fenil)- [(3S)- 3- amino- pirrolidin- 1- il]- metanona	1.2	Ver ejemplo		458
I- 176		[4- [6- amino- 5- (2,4- diclorobenciloxi)- piridin- 3- il]- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	0.85	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1,8 Hz, 1H), 7.71 (d, J = 3.5 Hz, 1 H), 7.50 (m, 5H), 7.30 (dd, J = 2.0 Hz, J = 8.3 Hz, 1H), 7.18 (d, J = 1.8 Hz, 1H), 5.22 (s, 2H), 4.83 (br s, 2H), 4.23 (m, 2H), 2.78 (m, 2H), 1.95 (m, 2H), 1.76 (m, 3H), 1.25 (m, 4H), 0.85 (m, 4H)	525

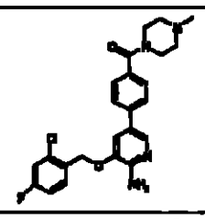
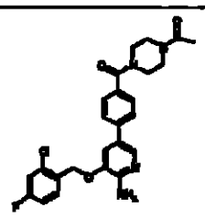
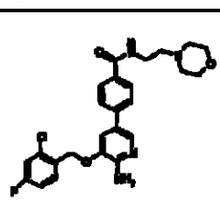
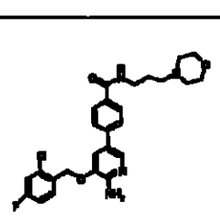
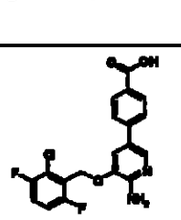
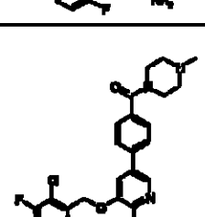
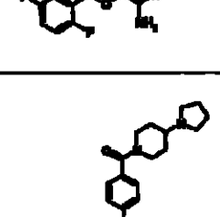
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 177		{4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona	0.79	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.50 (m, 6H), 7.30 (dd, J = 1.9 Hz, J = 8.3 Hz, 1H), 7.20 (s, 1H), 5.21 (s, 2H), 5.07 (br s, 2H), 3.65 (m, 4H), 2.45 (m, 4H), 2.36 (s, 3H)	473
I- 178		1(4- {4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- benzoil}- piperazin- 1- il)- etanona	1.67	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.97 (d, J = 1.8 Hz, 1H), 7.50 (m, 6H), 7.30 (dd, J = 2.0 Hz, J = 8.3 Hz, 1H), 7.18 (d, J = 1.8 Hz, 1H), 5.22 (s, 2H), 4.87 (br s, 2H), 3.64 (m, 4H), 3.53 (m, 4H), 2.14 (s, 3H)	501
I- 179		4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- N- (1- metil- piperidin- 4- il)- benzamida	1.12	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.98 (d, J = 1.8 Hz, 1H), 7.81 (d, J = 8.3 Hz, 2H), 7.55 (d, J = 8.3 Hz, 2H), 7.46 (m, 2H), 7.30 (dd, J = 2.0 Hz, J = 8.3 Hz, 1 H), 7.18 (d, J = 1.8 Hz, 1H), 6.09 (br d, 1H), 5.22 (s, 2H), 4.83 (br s, 2H), 4.05 (m, 1H), 3.06 (m, 1H), 2.46 (s, 3H), 2.32 (m, 1H), 2.12 (m, 1H), 1.83 (m, 1H), 1.26 (m, 2H), 0.88 (m, 2H)	486
I- 180		4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida	3.8	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.98 (d, J = 1.8 Hz, 1 H), 7.84 (d, J = 8.3 Hz, 2H), 7.56 (d, J = 8.3 Hz, 2H), 7.46 (m, 2H), 7.30 (dd, J = 2.0 Hz, J = 8.3 Hz, 1H), 7.20 (d, J = 1.8 Hz, 1H), 6.90 (br t, 1H), 5.22 (s, 2H), 4.91 (br s, 2H), 3.75 (m, 4H), 3.59 (m, 2H), 2.65 (m, 2H), 2.55 (m, 4H)	502
I- 181		4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- il- propil)- benzamida	2	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.99 (d, J = 1.7 Hz, 1H), 7.87 (d, J = 8.3 Hz, 2H), 7.71 (m, 1H), 7.55 (d, J = 8.3 Hz, 2H), 7.47 (m, 2H), 7.30 (dd, J = 2.0 Hz, J = 8.3 Hz, 1H), 7.21 (d, J = 1.7 Hz, 1H), 5,23 (s, 2H), 4.91 (br s, 2H), 3.75 (m, 4H), 3.59 (m, 2H), 2.60 (m, 6H), 1.83 (m, 2H)	516
I- 182		ácido 4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- benzoico		Ver ejemplo	(400 MHz, DMSO- d_6) δ 5.35 (s, 2H, CH_2), 5.95 (br s, 2H, NH_2), 7.40- 8.00 (multiples, 10H, aromaticos	388 (M+)

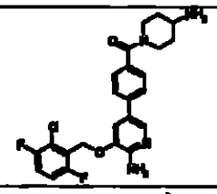
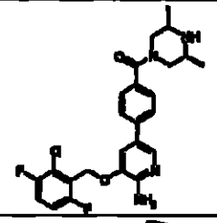
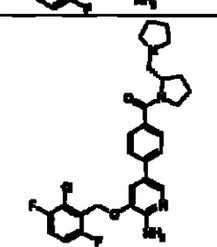
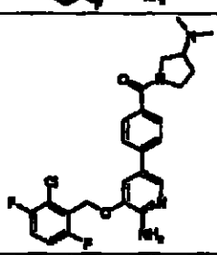
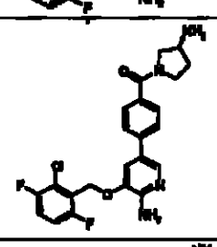
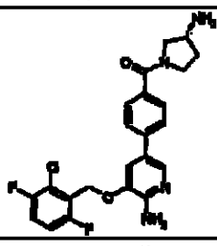
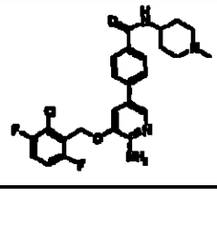
No.	Estructura	Nombre	Met IC_{20} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 183		{4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	0.75	Ver ejemplo	^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.7 Hz, 1H), 7.74 (d, J = 7.8 Hz, 1H), 7.68 (d, J = 7.7 Hz, 1H), 7.53 (m, 6H), 7.15 (d, J = 1.7 Hz, 1H), 5.35 (s, 2H), 4.82 (br s, 2H), 4.42 (m, 1H), 3.50 (m, 2H), 2.65 (m, 4H), 2.2- 1.5 (m, 10H)	525
I- 184		{4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	>20	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.7 Hz, 1H), 7.74 (d, J = 7.8 Hz, 1H), 7.66 (d, J = 7.7 Hz 1H), 7.53 (m, 6H), 7.15 (d, J = 1.7 Hz, 1H), 5.36 (s, 2H), 4.82 (br s, 2H), 4.42 (m, 1H), 3.50 (m, 2H), 2.65 (m, 4H), 2.2- 1.5 (m, 10H)	525
I- 185		{4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona	1.39	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.97 (d, J = 2.1 Hz, 1H), 7.74 (d, J = 7.8 Hz, 1 H), 7.68 (d, J = 7.7 Hz, 1H), 7.51 (m, 6H), 7.16 (d, J = 2.1 Hz, 1H), 5.35 (s, 2H), 4.88 (br s, 2H), 3.89 (m, 1H), 3.65 (m, 2H), 3.45 (m, 1H), 2.75 (m, 1H), 2.31 (s, 3H), 2.22 (s, 3H), 2.11 (m, 1H), 1.89 (m, 1H).	485
I- 186		[(3S)- 3- amino- pirrolidin- 1- il]- {4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- metanona	0.79	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.93 (d, J = 1.4 Hz, 1H), 7.74 (d, J = 7.7 Hz, 1H), 7.67 (d, J = 7.4 Hz, 1H), 7.55 (m, 3H), 7.45 (m, 3H), 7.15 (d, J = 1.4 Hz, 1H), 5.35 (s, 2H), 5.01 (br s, 2H), 3.65 (m, 4H), 2.03 (m, 3H), 1.75 (m, 1H), 0.85 (m, 1H)	457
I- 187		{4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	1.01	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.8 Hz, 1H), 7.74 (d, J = 7.9 Hz, 1H), 7.66 (m, 1H), 7.60 (m, 1H), 7.47 (m, 5H), 7.14 (d, J = 1.8 Hz, 1H), 5.35 (s, 2H), 4.81 (br s, 2H), 4.60 (m, 1H), 3.74 (m, 1H), 2.96 (m, 2H), 2.65 (m, 2H), 2.22 (m, 1H), 1.85 (m, 2H), 1.55 (m, 4H), 1.25 (m, 2H), 0.95 (m, 2H)	525
I- 188		{4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona	1.64	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.95 (d, J = 1.8 Hz, 1H), 7.74 (d, J = 7.7 Hz, 1H), 7.68 (d, J = 7.7 Hz, 1H), 7.60 (t, J = 7.7 Hz, 1H), 7.48 (m, 5H), 7,14 (d, J = 1.8 Hz, 1H), 5.35 (s, 2H), 4.89 (br s, 2H), 3.80 (m, 2H), 3.51 (m, 2H), 2.40 (m, 4H), 2.32 (s, 3H)	471

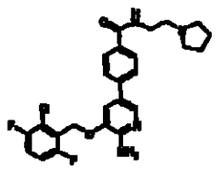
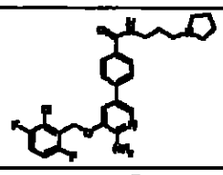
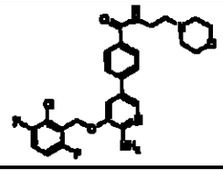
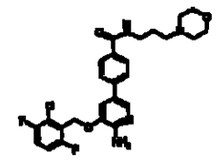
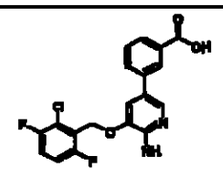
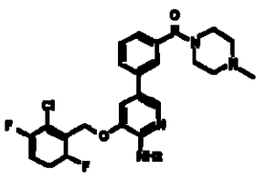
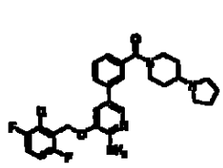
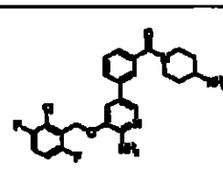
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^1H- NMR	MS m/z (M+1)
I- 189		1- (4- {4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- benzoil}- piperazin- 1- il)- etanona	6.7	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.8 Hz, 1H), 7.74 (d, J = 7.7 Hz, 1H), 7.68 (d, J = 7.7 Hz, 1H), 7.60 (t, J = 7.7 Hz, 1H), 7.48 (m, 5H), 7.14 (d, J = 1.8 Hz, 1H), 5.36 (s, 2H), 4.87 (br s, 2H), 3.64 (m, 4H), 3.53 (m, 4H), 2.14 (s, 3H)	499
I- 190		{4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- N- (1- metil- piperidin- 4- il)- benzamida	3.8	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.98 (d, J = 1.8 Hz, 1H), 7.79 (d, J = 8.3 Hz, 2H), 7.74 (d, J = 7.8 Hz, 1H), 7.67 (d, J = 7.6 Hz, 1H), 7,60 (m, 1H), 7.52 (m, 3H), 7.14 (d, J = 1.8 Hz, 1H), 5,98 (m, 1H), 5.36 (s, 2H), 4.85 (br s, 2H),), 4.05 (m, 1H), 2.90 (m, 2H), 2.32 (s, 3H), 2.18 (m, 2H), 2.01 (m, 2H), 1.62 (m, 2H)	485
I- 191		4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida	5.2	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.98 (d, J = 1.8 Hz, 1H), 7.82 (d, J = 8.4 Hz, 2H), 7.74 (d, J = 7.8 Hz, 1H), 7.68 (d, J = 7.7 Hz, 1H), 7.60 (t, J = 7.7 Hz, 1H), 7.53 (m, 3H), 7.17 (d, J = 1.8 Hz, 1H), 6.83 (m, 1H), 5.36 (s, 2H), 4.89 (br s, 2H), 3.74 (m, 4H), 3.57 (m, 2H), 2.62 (m, 2H), 2.52 (m, 4H)	501
I- 192		4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida	3.8	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.98 (d, J 1.8 Hz, 1H), 7.95 (m, 1H), 7.86 (d, J = 8,4 Hz, 2H), 7.74 (d, J = 7.7 Hz, 1H), 7.68 (d, J = 7.7 Hz, 1H), 7.60 (t, J = 7.7 Hz, 1H), 7.53 (m, 3H), 7.17 (d, J = 1.8 Hz, 1H), 5.36 (s, 2H), 4.94 (br s, 2H), 3.75 (m, 4H), 3.59 (m, 2H), 2.59 (m, 6H), 1.83 (m, 2H)	515
I- 193		ácido 4- [6- amino- 5- (4- *terc*- butil- benciloxi)- piridin- 3- il]- benzoico		Ver ejemplo	(400 MHZ, DMSO- d_6) δ 1.25 (s, 9H, t- butil), 5.20 (s, 2H, CH_2), 5.95 (br s, 2H, NH_2), 7.35- 8.00 (multiples, 10H, aromaticos	376 (M+)
I- 194		{4- [6- amino- 5- (4- *terc*- butil- benciloxi)- piridin- 3- il]- fenil}- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	1.89	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.94 (d, J = 1.7 Hz, 1H), 7.49 (m, 8H), 7.21 (d, J = 1.7 Hz, 1H), 5.11 (s, 2H), 4.80 (br s, 2H), 4.48 (m, 1H), 3.48 (m, 2H), 2.62 (m, 4H), 2.2- 1.5 (m, 10H), 1.34 (s, 9H)	513

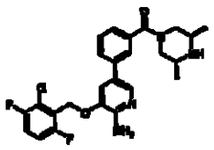
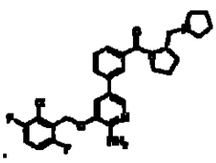
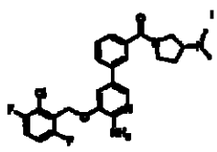
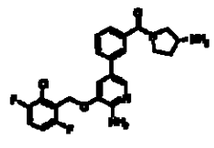
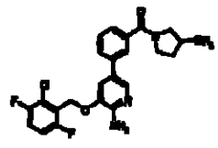
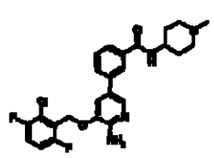
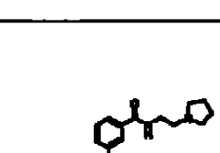
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 195		{4- [6- amino- 5- (4- *tert*- butil- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	3.27	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.94 (d, J = 1.7 Hz, 1H), 7.49 (m, 8H), 7.21 (d, J = 1.7 Hz, 1H), 5.11 (s, 2H), 4.80 (br s, 2H), 4.48 (m, 1H), 3.48 (m, 2H), 2.62 (m, 4H), 2.2- 1.5 (m, 10H), 1.34 (s, 9H)	513
I- 196		{4- [6- amino- 5- (4- *tert*- butil- benciloxi)- piridin- 3- il]- fenil}- [(3R)- 2- dimetilamino- pirrolidin- 1- il]- metanona	4.29	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.94 (d, J = 2.1 Hz, 1H), 7.54 (m, 4H), 7.45 (d, J = 8.3 Hz, 2H), 7.38 (d, J = 8.3 Hz, 2H), 7.21 (d, J = 1.7 Hz, 1H), 5.11 (s, 2H), 4.84 (br s, 2H), 3.89 (m, 1H), 3.64 (m, 2H), 3.42 (m, 1H), 2.70 (m, 1H), 2.31 (s, 3H), 2.22 (s, 3H), 2.05 (m, 1H), 1.89 (m, 1H), 1.34 (s, 9H)	473
I- 197		{4- [6- amino- 5- (4- *tert*- butil- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il]- metanona	3.8	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.93 (d, J = 1.7 Hz, 1H), 7.48 (m, 4H), 7.41 (m, 4H), 7.21 (d, J = 1.7 Hz, 1H), 5.11 (s, 2H), 4.85 (br s, 2H), 3.80 (m, 2H), 3.52 (m, 2H), 2.41 (m, 4H), 2.33 (s, 3H), 1.34 (s 9H)	459
I- 198		1- (4- {4- [6- amino- 5- (4- *tert*- butil- benciloxi)- piridin- 3- il]- benzoil}- piperazin- 1- il)- etanona	3	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.94 (d, J = 1.8 Hz, 1H), 7.50 (m, 8H), 7.21 (d, J = 1.7 Hz, 1H), 5.11 (s, 2H), 4.90 (br s, 2H), 3.64 (m, 4H), 3.53 (m, 4H), 2.14 (s, 3H), 1.34 (s, 9H)	487
I- 199		4- [6- amino- 5- (4- *tert*- butil- benciloxi)- piridin- 3- il]- N- (1- metil- piperidin- 4- il)- benzamida	2.92	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.95 (d, J = 1.8 Hz, 1H), 7.80 (d, J = 8.3 Hz, 2H), 7.54 (d, J = 8.3 Hz, 2H), 7.44 (d, J = 7.7 Hz, 2H), 7.38 (d, J = 7.7 Hz, 2H),7.21 (d, J = 1.8 Hz, 1H), 6.05 (m, 1H), 5.11 (s, 2H), 4.80 (br s, 2H), 4.01 (m, 1H), 2.84 (m, 2H), 2.33 (s, 3H) 2.20 (m, 2H), 2.10 (m, 2H), 1.82 (m, 2H), 1.34 (s, 9H)	487
I- 200		4- [6- amino- 5- (4- *tert*- butil- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida	6.88	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.95 (d, J = 1.8 Hz, 1H), 7.82 (d, J = 8.3 Hz, 2H), 7.54 (d, J = 8.3 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 7.38 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 1.8 Hz, 1H), 6.91 (t, J = 4.6 Hz, 1H), 5.10 (s, 2H), 4.90 (br s, 2H), 3.74 (m, 4H), 3.57 (m, 2H), 2.62 (m, 2H), 2.51 (m, 4H), 1.34 (s, 9H)	489

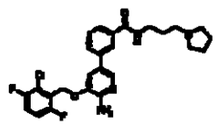
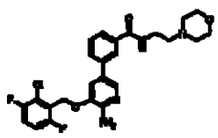
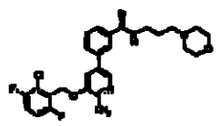
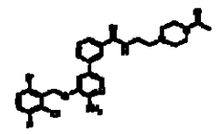
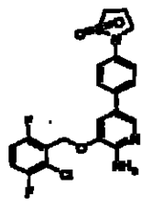
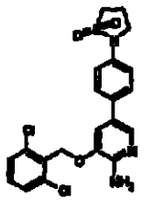
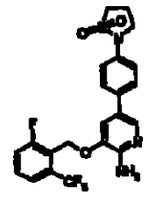
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 201		4- [6- amino- 5- (4- *tert*- butil- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- il- propil)- benzamida	6.3	Ver ejemplo	(300 MHz, $CDCl_3$) δ 8.01 (t, J = 4.5 Hz, 1H), 7.96 (d, J = 1.8 Hz, 1H), 7.86 (d, J = 8.3 Hz, 2H), 7.54 (d, J = 8.3 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 7.38 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 1.8 Hz, 1H), 5.12 (s, 2H), 4.89 (br s, 2H), 3.74 (m, 4H), 3.59 (m, 2H), 2.56 (m, 6H), 1.82 (m, 2H), 1.34 (s, 9H)	503
I- 202		Ácido 4- [6- amino- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- benzoico		Ver ejemplo	(400 MHz, $CDCl_3$) δ 5.25 (s, 2H, CH_2), 5.80 (br s, 2H, NH_2), 7.20 - 8.00 (multiples, 9H, aromaticos)	374
I- 203		{4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	1.48	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.97 (d, J = 1,7 Hz, 1H), 7.52 (m, 6H), 7.20 (m, 1H), 7.05 (m, 1H), 5.21 (s, 2H), 4.80 (br s, 2H), 4.45 (m, 1H), 3.52 (m, 2H), 2.76 (m, 4H), 2.2- 1.5 (m, 10H)	509
I- 204		{4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	2.5	Ver ejemplo	(300 MHz, CDC13) δ 7.97 (d, J = 1.7 Hz, 1H), 7.52 (m, 6H), 7.20 (m, 1H), 7.05 (m, 1H), 5.21 (s, 2H), 4.80 (br s, 2H), 4.45 (m, 1H), 3.52 (m, 2H), 2.76 (m, 4H), 2.2- 1.5 (m, 10H)	509
I- 205		{4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona	6.1	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.52 (m, 6H), 7.20 (m, 1H), 7.04 (m, 1H), 5.21 (s, 2H), 4.95 (br s, 2H), 3.90 (m, 1H), 3.61 (m, 2H), 3.33 (m, 1H), 2.75 (m, 1H), 2.32 (s, 3H), 2.23 (s, 3H), 2.10 (m, 1H), 1.89 (m, 1H)	469
I- 206		{4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il]- metanona	1.83	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.97 (d, J = 1.8 Hz, 1H), 7.52 (m, 6H), 7.20 (m, 1H), 7.04 (m, 1H), 5.21 (s, 2H), 4.84 (br s, 2H), 3.84 (m, 4H), 2.15 (m, 1H), 1.76 (m, 2H), 1.56 (m, 2H)	441

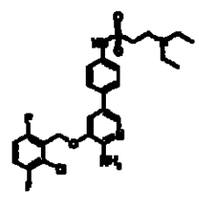
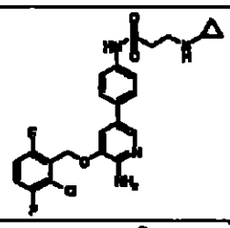
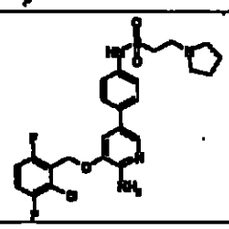
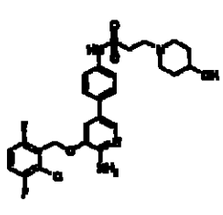
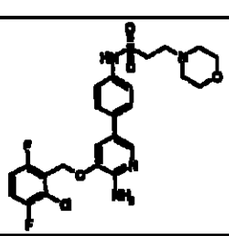
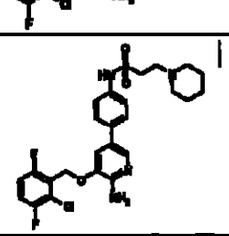
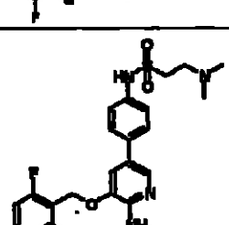
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 207		{4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- fenil}- (4- 3- metil- piperazin- 1- il]- metanona	5	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.52 (m, 6H), 7.20 (m, 1H), 7.04 (m, 1H), 5.21 (s, 2H), 4.89 (br s, 2H) 3.80 (m, 2H), 3.65 (m, 2H), 2.43 (m 4H), 2.33 (s, 3H)	456
I- 208		1- (4- {4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- benzoil}- piperazin- 1- il)- etanona	5.3	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.52 (m, 6H), 7.20 (m, 1H), 7.04 (m, 1H), 5.21 (s, 2H), 4.90 (br s, 2H), 3.67 (m, 4H), 3.53 (m, 4H), 2.22 (s, 3H)	483
I- 209		4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida	11	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.99 (d, J = 1.6 Hz, 1H), 7.84 (d, J = 8.3 Hz, 2H). 7.57 (d, J = 8.3 Hz, 2H), 7.49 (dd, J = 6.0 Hz, 8.5 Hz, 1H), 7.20 (m, 2H), 7.04 (m, 1H), 6.82 (m, 1H), 5.22 (s, 2H), 4.85 (br s, 2H), 3.74 (m, 4H), 3.58 (m, 2H), 2.63 (m, 2H), 2.53 (m, 4H)	485
I- 210		4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- il- propil)- benzamida	5.8	Ver ejemplo	(300 MHz, $CDCl_3$) δ 8.06 (m, 1 H), 7.00 (d, J = 1.6 Hz, 1H), 7.89 (d, J = 8.3 Hz, 2H), 7.55 (d, J = 8.3 Hz, 2H), 7.49 (dd, J = 6.0 Hz, 8.5 Hz, 1H), 7.20 (m, 2H), 7.04 (m, 1H), 5.22 (s, 2H), 4.85 (br s, 2H), 3.75 (m, 4H), 3.60 (m, 2H), 2.55 (m, 6H), 1.83 (m, 2H)	499
I- 211		ácido 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzoico	0.35	Ver ejemplo	(300 MHz, DMSO- d_6) δ 5.21 (s, 2H), 5.71 (s, 2H), 7.31- 7.46 (m, 1H), 7.5- 7.62 (m, 4H), 7.91- 7.94 (m, 3H).	
I- 212		{4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- etil)- metanona	0.063	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.97 (d, J = 1.6 Hz, 1H), 7.56 (d, J = 8.2 Hz, 2H), 7.48 (d, J = 8.2 Hz, 2H), 7.35 (d, J = 1.6 Hz, 1H), 7.20 (m, 1H), 7.06 (m, 1H), 5.29 (s, 2H), 4.81 (br s, 2H), 3.79 (m, 2H), 3.54 (m, 2H), 3.44 (m, 4H), 2.33 (s, 3H)	473
I- 213		{4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	0.049	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.97 (d, J = 1.7 Hz, 1H). 7.55 (d, J = 8.2 Hz, 2H), 7.45 (d, J = 8.2 Hz, 2H), 7.35 (d, J = 1.6 Hz, 1H), 7.20 (m, 1H), 7.06 (m, 1H). 5.29 (s, 2H), 4.79 (br s, 2H), 4.60 (m, 1H), 3.85 (m, 1H), 3.02 (m, 2H), 2.65 (m, 4H), 2.35 (m, 1H), 2.05 (m, 4H), 1.65 (m, 4H).	527

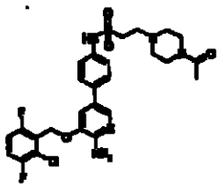
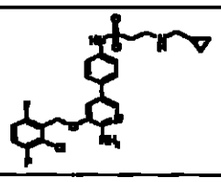
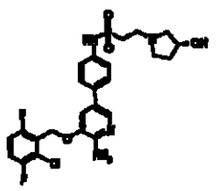
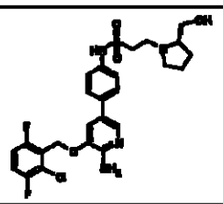
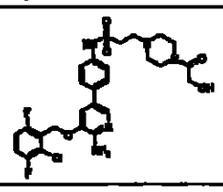
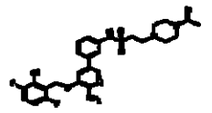
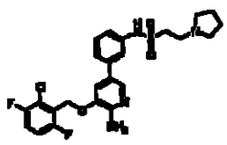
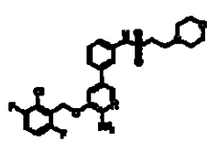
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 214		{4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (4- amino- piperidin- 1- il)- metanona	0.1	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.92 (s, 1H), 7.66 (m, 4H), 7.46 (m, 4H), 5.89 (s, 2H), 5.39 (s, 2H), 4.19 (m, 1H), 3.50 (m, 2H), 2.54 (m, 5H), 1.95 (m, 2H), 1.83 (m, 3H), 1.64 (m, 4H)	MS (ES+) m/z 543 (MH+). MS m/z 473 [M+1]
I- 215		{4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona	0.1	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.98 (s, 1H), 7.58 (d, 2H), 7.41 (d, 2H), 7.31 (s, 1H), 7.19 (m, 1H), 7.06 (m, 1H), 5.31 (s, 2H), 4.81 (m, 2H), 4.68 (m, 1H), 3.99 (m, 1H), 2.89 (m, 2H), 2.69 (m, 1H), 2.40 (m, 1H), 1.74 (m, 1H) 1.18 (d, 6H)	487
I- 216		{4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	0.1	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.95 (d, 1H), 7.69 (d, 2H), 7.58 (m, 2H), 7.50 (d, 2H), 7.40 (m, 1H), 5.81 (s, 2H), 5.29 (s, 2H), 4.35 (m, 1H), 3.5 (d, 2H), 2,87 (d, 2H), 2.71 (d, 2H), 1.7- 2.0 (m, 10H)	527
I- 217		{4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona	0.12	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.97 (s, 1H), 7.60 (m, 4H), 7.32 (s, 1H), 7.18 (m, 1H), 7.04 (m 1H), 5.31 (s, 2H), 4.78 (m, 2H), 3.90 (m, 1H), 3.68 (m, 2H), 3.41 (m, 1H), 2.78 (m, 1H), 2.31 (s, 3H), 2.24 (s, 3H), 2.04 (m, 1H), 1.84 (m, 1H)	487
I- 218		{4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(3R)- 3- amino- pirrolidin- 1- il]- metanona	0.053	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.84 (s, 1H), 7.62 (m, 5H), 7.35 (m, 1H), 7.20 (m, 1H), 5.38 (s, 2H), 3.78 (m, 3H), 3.55 (m, 1H), 3.41 (m, 1H), 2.18 (m, 1H), 1.82 (m, 1H)	459
I- 219		{4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il]- metanona	0.095	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.84 (s, 1H), 7.62 (m, 5H), 7,35 (m, 1H), 7.20 (m, 1H), 5.38 (s, 2H), 3.78 (m, 3H), 3.55 (m, 1H), 3.41 (m, 1H), 2.18 (m, 1H), 1,82 (m, 1H)	459
I- 220		4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (1- metil- piperidin- 4- il)- benzamida	0.11	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.97 (s, 1H), 7.80 (d, 2H), 7,58 (d, 2H), 7.36 (s, 1H), 7.18 (m, 1H), 7.04 (m, 1H), 6.01 (d, 1H), 5.28 (s, 2H), 4.78 (s, 2H), 3.98 (m, 1H), 2.85 (m, 2H), 2.31 (s, 3H), 2.18 (t, 2H), 2.10 (m, 2H), 1.65 (m, 2H)	487

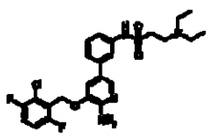
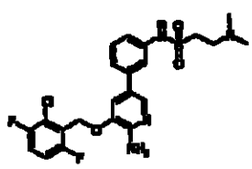
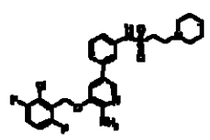
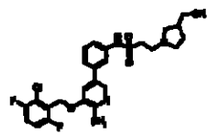
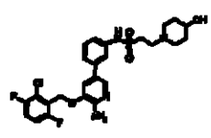
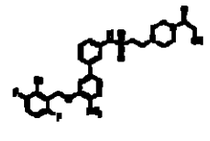
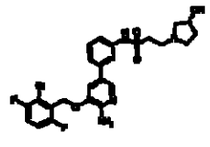
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 221		{4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (1- metila- piperidin- 4- il)- benzamida	0.18	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7,98 (s, 1H), 7.89 (d, 2H), 7.56 (d, 2H), 7.45 (m, 1H), 7.31 (s, 1H), 7.17 (m, 1H), 7.01 (m, 1H), 5.28 (s, 2H), 4.85 (s, 2H), 3.65 (m, 2H), 2.89 (t, 2H), 2.76 (m, 4H), 1.89 (m, 4H)	487
I- 222		{4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (3- pirrolidin- 1- il- propil)- benzamida	0.19	Ver ejemplo	(400 MHz, DMSO- d_6) δ 8.72 (m, 1H), 7.95 (m,3H), 7.57 (d, 2H), 7.35 (s, 1H), 7.18 (m, 1H), 7.02 (m, 1H), 5.31 (s, 2H), 4.79 (s, 2H), 3.68 (m, 2H), 2.89 (m, 6H), 1.97 (m, 6H)	501
I- 223		4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida	0.165	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.97 (s, 1H), 7.82 (d, 2H), 7.62 (d, 2H), 7.36 (s, 1H), 7.18 (m, 1H), 7.05 (m, 1H), 6.81 (m, 1H), 5.28 (s, 2H), 4.79 (s, 2H), 3.78 (m, 4H), 3.58 (m, 2H), 2.63 (t, 2H), 2.51 (m, 4H)	503
I- 224		4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- il- propil)- benzamida	0.28	Ver ejemplo	(400 MHz, DMSO- d_6) δ 8.04 (m, 1H), 7.96 (s, 1H), 7.89 (d, 2H), 7.58 (d, 2H), 7.38 (s, 1H), 7.18 (m, 1H), 7.06 (m, 1H), 7.29 (s, 2H), 4.81 (s, 2H), 3.76 (m, 4H), 3.61 (m, 2H), 2.59 (t, 2H), 2.54 (m, 4H), 1.79 (m, 2H)	517
I- 225		ácido 3- [6- amino- 5- (2- cloro- 3,6- difluoro- , benciloxi)- piridin- 3- il]- benzoico	3.7/0.6	Ver ejemplo	(300 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.92 (s, 1H), 7.84 (d, J = 7,4 Hz, 1H), 7.60 (m, 2H), 7.55 (s, 1H), 7.40 (m, 2H), 5.75 (s, 2H), 5.31 (br s, 2H)	391
I- 226		3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona	0.068	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.7 Hz, 1H), 7.58 (dd, J = 1.1 Hz, 6.8 Hz, 1H), 7.46 (m, 1H), 7. 35 (m, 3H), 7.20 (m, 1H), 7.06 (m, 1H), 5.27 (s, 2H), 4.81 (br s, 2H), 3.83 (m, 2H), 3.50 (m, 2H), 2.49 (m, 2H), 2.39 (m, 2H), 2.33 (s, 3H)	473
I- 227		{3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	0.05	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.8 Hz, 1H), 7.57 (dd, J = 1.2 Hz, 8.0 Hz, 1H), 7.45 (t, J = 7.6 Hz, 1H), 7.34 (m, 3H), 7.20 (m, 1H), 7.06 (m, 1H), 5.27 (s, 2H), 4.77 (br s, 2H), 4.60 (m, 1H), 3.80 (m, 1H), 3.02 (m, 2H), 2.60 (m, 2H), 2.30 (m, 1H), 1.95 (m, 2H), 1.85 (m, 4H), 1.65 (m, 4H)	527
I- 228		{3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (4- amino- piperidin- 1- il) - metanona	0.23	Ver ejemplo	(300 MHz, CD- $_3$ OD) δ 8.01 (s, 1H), 7.89 (s, 1H), 7.75 (m, 2H), 7.59 (s, 1H), 7.48 (t, 1H), 7.31 (m, 1H), 7.18 (m, 1H), 5.38 (s, 2H), 4.01 (m, 1H), 3.09 (m, 2H), 2.68 (t, 2H), 1.97 (m, 2H), 1.58 (m, 2H)	473

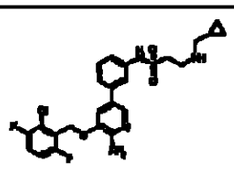
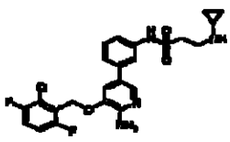
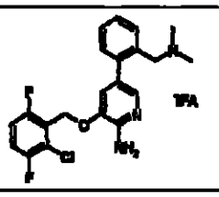
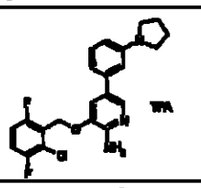
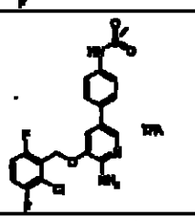
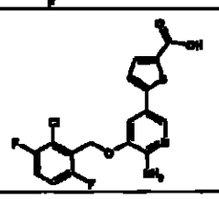
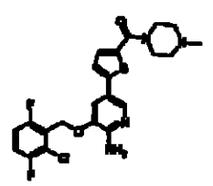
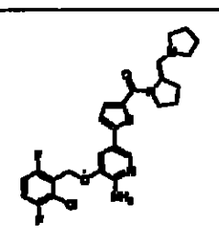
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 229		{3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona	0.066/ 0.18	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1,7 Hz, 1H), 7.56 (m, 1H), 7.47 (t, J = 7.6 Hz, 1H), 7.36 (m, 3H), 7.20 (m, 1H), 7.06 (m, 1H), 5.27 (s, 2H), 4.82 (br s, 2H), 4.68 (m, 1H), 3.65 (m, 1H), 3.90 (m, 2H), 2.70 (m, 1H), 2.40 (m, 1H), 1.97 (m, 1H), 1.15 (d, 3H), 0.99 (d, 3H)	487
I- 230		{3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	0.19	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.7 Hz, 1H), 7.66 (s, 1H), 7.57 (d, J = 6.8 Hz, 1H), 7.45 (m, 2H), 7.36 (d, J = 1.7 Hz, 1H), 7.20 (m, 1H), 7.06 (m, 1H), 5.27 (s, 2H), 4.78 (br s, 2H), 4.42 (m, 1H), 3.45 (m, 2H), 2.68 (m, 4H), 2.2- 1.5 (m, 10H)	527
I- 231		{3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona	0.128	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7,96 (s, 1H), 7.68 (d, J = 7.4 Hz, 1H), 799 (m, 1H), 7.44 (m, 2H), 7.36 (s, 1H), 7.20 (m, 1H), 7.06 (m, 1H), 5.27 (s, 2H), 4.80 (br s, 2H), 3.90 (m, 1H), 3.61 (m, 2H), 3.41 (m, 1H), 2.77 (m, 1H), 2.32 (s, 3H), 2.22 (s, 3H), 2.10 (m, 1H), 1.82 (m, 1H)	487
I- 232		{3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(3R)- 3- amino- pirrolidin- 1- il]- metanona	0.12	Ver ejemplo	(300 MHz, CD_3OD) δ 7.86 (m, 1H), 7.75 (m, 2H), 7,58 (m, 3H), 7.38 (m, 1H), 7.22 (m, 1H), 5.38 (s, 2H), 4.00- 3.56 (m, 5H), 2.40 (m, 1H), 2.12 (m, 1H)	459
I- 233		{3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- amino- pirrolidin- 1- il]- metanona	0.12	Ver ejemplo	(300 MHz, CD_3OD) δ 7.86 (s, 1H), 7.75 (m, 2H), 7.58 (m, 3H), 7.38 (m, 1H), 7.22 (m, 1H), 5.38 (s, 2H), 4.00- 3.56 (m, 5H), 2.40 (m, 1H), 2.12 (m, 1H).	459
I- 234		{3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- N- (1- metil- piperidin- 4- il)- benzamida	0.23	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.96 (d, J = 1.7 Hz, 1H), 7.94 (s, 1H), 7.64 (m, 2H), 7.47 (t, J = 7.7 Hz, 1H), 7.37 (d, J = 1.7 Hz, 1H), 7.20 (m, 1H), 7.06 (m, 1H), 6.25 (m, 1H), 5.27 (s, 2H), 4.81 (br s, 2H), 3.99 (m, 1H), 2.84 (m, 2H), 2.30 (s, 3H), 2.16 (m, 2H), 2.04 (m, 2H), 1.64 (m, 2H)	487
I- 235		{3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- N- (2- pirrolidin- 1- il- etil)- benzamida	0.26	Ver ejemplo	(300 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.96 (d, J = 1.7 Hz, 1H), 7.72 (d, J = 7.7 Hz, 1H), 7.64 (d, J =7.8 Hz, 1H), 7.47 (t, J = 7.7 Hz, 1H), 7.40 (d, J = 1.7 Hz, 1H), 7.20 (m, 2H), 7.06 (m, 1H), 5.27 (s, 2H), 4.83 (br s, 2H), 3.61 (m, 2H), 2.77 (m, 2H), 2.62 (m, 4H), 1.81 (m, 4H)	487

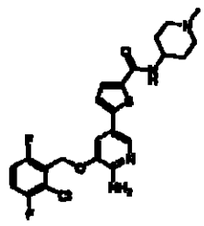
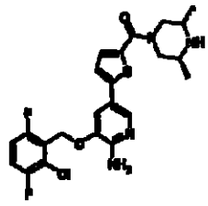
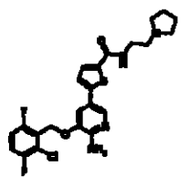
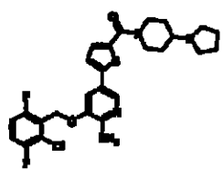
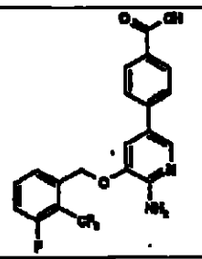
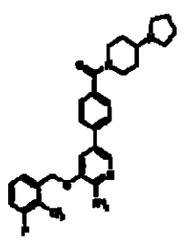
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 236		{3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- N- (3- pirrolidin- 1- il- propil)- benzamida	0.28	Ver ejemplo	(300 MHz, $CDCl_3$) δ 8.78 (m, 1H), 8.04 (d, J = 1.6 Hz, 1H), 7.98 (d, J = 1.6 Hz, 1H), 7.68 (d, J = 7.7 Hz, 1H), 7.63 (d, J = 7.9 Hz, 1H), 7.45 (t, J = 7.7 Hz, 1H), 7.43 (d, J = 1.6 Hz, 1H), 7.20 (m, 1H), 7.06 (m, 1H), 5.29 (s, 2H), 4.77 (br s, 2H), 3.61 (m, 2H), 2.77 (m, 2H), 2.66 (m, 4H), 1.87 (m, 2H), 1.80 (m, 4H)	501
I- 237		{3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- N- (2- morfolin- 4- il- etil)- benzamida	0.35	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.89 (t, J = 1.5 Hz, 1H), 7.97 (d, J =1.8 Hz, 1H), 7.66 (m, 2H), 7.49 (t, J = 7.7 Hz, 1H), 7.38 (d, J = 1,8 Hz, 1H), 7.20 (m, 1H), 7.06 (m, 2H), 5.27 (s, 2H), 4.85 (br s, 2H), 3.72 (m, 4H), 3.59 (m, 2H), 2.63 (m, 2H), 2.52 (m, 4H)	503
I- 238		3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- il- propil)- benzamida	0.35	Ver ejemplo	(300 MHz, $CDCl_3$) δ 8.02 (m, 2H), 7.97 (d, J = 1.8 Hz, 1H), 7.68 (d, J = 7.8 Hz, 1H), 7.65 (d, J = 8.3 Hz, 1H), 7.48 (t, J = 7.7 Hz, 1H), 7.38 (d, J = 1,8 Hz, 1H), 7.19 (m, 1H), 7.06 (m, 1H), 5.27(s, 2H), 4.81 (br s, 2H), 3.66 (m, 4H), 3.59 (m, 2H), 2.55 (m, 2H), 2.49 (m, 4H), 1.81 (m, 2H)	517
I- 239		N- [2- (4- acetil- piperazin- 1- il)- etil]- 3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzamida	0.1	Ver ejemplo	(300 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.86 (s, 1H), 7.67 (dd, 2H), 7.56 (t, 1H), 7.48 (s, 1H), 7.21 (m, 1H), 7.08 (m, 1H), 6.02 (br s, 2H), 5.39 (s, 2H), 3.75 (m, 4H), 3.60 (m, 2H), 2.79 (m, 2H), 2.60 (m, 4H), 2.11 (s, 3H)	544
I- 240		3- (2- cloro- 3,6- difluoro- benciloxi)- 5- [4- (1,1- dioxo- 1λ^6- isotizolidin- 2- il)- fenil]- piridin- 2- ilamina	0.1	Ver ejemplo	(400 MHz, DMSO- d_6) δ 7.88 (s, 1H), 7.62 (d, 2H), 7.56 (m, 1H), 7.51 (s, 1H), 7.40 (m, 1H), 7.23 (d, 2H), 5.70 (s, 2H), 5.28 (s, 2H), 3.78 (t, 2H), 3.49 (t, 2H), 2.41 (t, 2H)	466
I- 241		3- (2,6- dicloro- benciloxi)- 5- [4- (1,1- dioxo- 1λ^6- isotizolidin- 2- il)- fenil]- piridin- 2- ilamina	0.067	Ver ejemplo		464
I- 242		5- [4- (1,1- dioxo- 1λ^6- isotizolidin- 2- il)- fenil]- 3- (2- fluoro- 6- trifluorometil- benciloxi)- piridin- 2- ilamina	0.14	Ver ejemplo		482

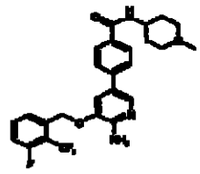
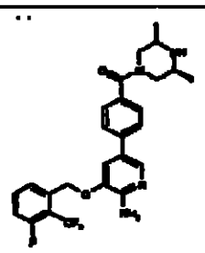
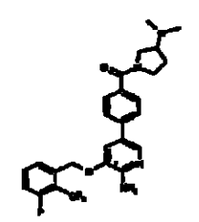
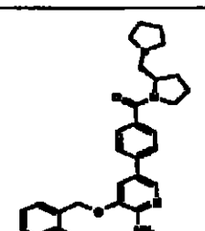
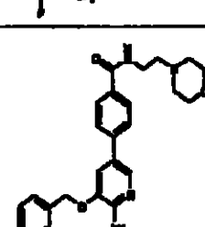
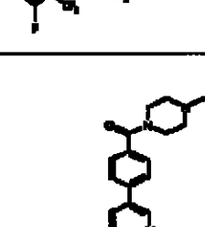
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 243		2- dietilamino- ácido etanosulfonico {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	0.043	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.92 (d, J = 1.8 Hz, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 1.8 Hz, 1H), 7.24 (m, 3H), 7.20 (m, 1H), 7.07 (m, 1H), 5.28 (s, 2H), 4.70 (br s, 2H), 3.22 (t, J = 6.1 Hz, 2H), 3.04 (t, J = 6.1 Hz, 2H), 2.65 (q, J = 7.1 Hz, 4H), 1.10 (t, J = 7.1 Hz, 6H)	525
I- 244		2- ciclopropilamino- ácido etanosulfonico {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	0.081	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.92 (d, J = 1.8 Hz, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 1.8 Hz, 1H), 7.24 (m, 3H), 7.20 (m, 1H), 7.07 (m, 1H), 5.28 (s, 2H), 4.75 (br s, 2H), 3.25 (s, 4H), 2.17 (m, 1H), 0.9 (m, 1H), 0.50 (m, 2H), 0.40 (m, 2H)	509
I- 245		2- pirrolidin- 1- il- ácido etanosulfonico {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	0.082	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.92 (d, J = 1.8 Hz, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7.31 (d, J = 1.8 Hz, 1H), 7.24 (m, 3H), 7.20 (m, 1H), 7.07 (m, 1H), 5.28 (s, 2H), 4.72 (br s, 2H), 3.27 (m, 2H), 3.06 (m, 2H), 2.59 (m, 4H), 1.86 (m, 4H)	523
I- 246		2- (4- hidroxi- piperidin- 1- il)- ácido etanosulfonico {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	0.135	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.92 (d, J = 1.8 Hz, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7.32 (m, 2H), 7.24 (m, 2H), 7.20 (m, 1H), 7.07 (m, 1H), 5.28 (s,2H), 4.74 (br s, 2H), 3.81 (m, 1H), 3.31 (t, 2H), 2.98 (t, 2H), 2.85 (m, 2H), 2.32 (m, 2H), 1.98 (m, 2H), 1.68 (m, 3H)	553
I- 247		2- morfolin- 4- il- ácido etanosulfonico {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	0.31	Ver ejemplo	(300 MHz, DMSO- d_6) δ 9.80 (br s, 1H), 7.89 (d, J = 1,6 Hz, 1H), 7.59 (m, 3H), 7.52 (d, J = 1.6 Hz, 1H), 7.26 (d, J = 8.6 Hz, 2H), 5.72 (br s, 2H), 5.28 (s, 2H), 3.49 (m, 4H), 3.28 (t, 2H), 2.69 (t, 2H), 2.31 (m, 4H)	539
I- 248		2- piperidin- 1- il- ácido etanosulfonico {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	0.114	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.93 (d, J = 1.8 Hz, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7.30 (m, 2H), 7.24 (m, 2H), 7.20 (m, 1H), 7.07 (m, 1H), 5.28 (s, 2H), 4.70 (br s, 2H), 3.25 (t, 2H), 2.92 (t, 2H), 2.52 (m, 4H), 1.85 (m, 4H), 1.63 (m, 2H)	537
I- 249		2- dimetilamino- ácido etanosulfonico {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	0.098	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.92 (d, J = 1.8 Hz, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7.30 (m, 2H), 7.24 (m, 2H), 7.20 (m, 1H), 7.07 (m, 1H), 5.28 (s, 2H), 4.71 (br s, 2H), 3.20 (t, 2H), 2.88 (t, 2H), 2,32 (s, 6H)	497

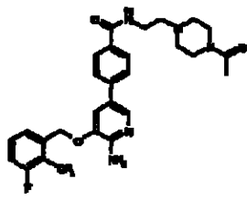
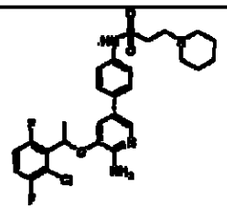
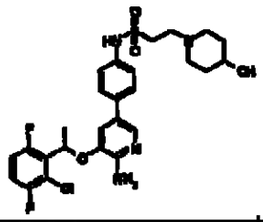
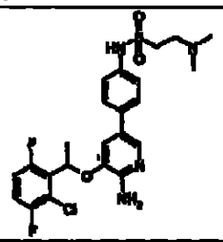
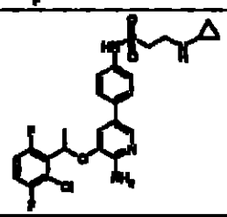
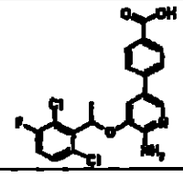
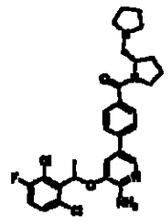
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^1H- NMR	MS m/z (M+1)
I- 250		2- (4- acetil- piperazin- 1- il) ácido etanosulfonico {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	0.42	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.92 (d, J = 1.8 Hz, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7,30 (m, 2H), 7.24 (m, 1H) 7.20 (m, 1H), 7.07 (m, 2H), 5.28 (s, 2H), 4.80 (br s, 2H), 3.65 (m, 2H), 3.48 (m, 2H), 3.32 (t, 2H), 2.94 (t, 2H), 2.50 (m, 2H) 2.46 (m, 2H), 2.10 (s, 3H)	580
I- 251		2- (ciclopropilmetil- amino) ácido etanosulfonico {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	0.075	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.48 (m, 2H), 7.31 (m, 3H), 7.21 (m, 1H), 7.18 (m, 1H), 5.28 (s, 2H), 4.75 (s, 2H), 3.23 (m, 4H), 2.58 (m, 2H), 1.00 (m, 1H), 0.56 (m, 2H), 0.18 (m, 2H)	523
I- 252		2- [(3R)- 3- hidroxi- pirrolidin- 1- il]- ácido etanosulfonico {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	0.125	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.43 (m, 2H), 7.31 (m, 3H), 7.19 (m, 1H), 7.05 (m, 1H), 5.28 (s, 2H), 4.75 (s, 2H), 4.45 (m, 1H), 3.29 (m, 2H), 3.10 (m, 3H), 2.88 (m, 1H), 2.61 (m, 1H), 2.30 (m, 2H), 1.89 (m, 2H)	539
I- 253		2- [(2S)- 2- hidroximetil- pirrolidin- 1- il]- ácido etanosulfonico {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida e	0.097	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.45 (m, 2H), 7.30 (m, 3H), 7.21 (m, 1H), 7,08 (m, 1H), 5.31 (s, 2H), 4.78 (s, 2H), 3.55 (m, 2H), 3.36 (t, 1H), 3.11 (m, 2H), 2.69 (m, 2H), 2.21 (m, 1H), 1.89 (m, 6H)	553
I- 254		2- [4- (2- hidroxi- acetil)- piperazin- 1- il]- ácido etanosulfonico {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	0.18	Ver ejemplo	(300 MHz, DMSO- d_6) δ 9.81 (s, 1H), 7.89 (s, 1H), 7.58 (d, 2H), 7.50 (s, 1H), 7.39 (m, 2H), 7.24 (d, 2H), 5.75 (s, 2H), 5.28 (s, 2H), 4.54 (t, 1H), 4.01 (d, 2H), 3.29 (m, 6H), 2.79 (t, 2H), 2.36 (m, 4H)	596
I- 255		2- (4- acetil- piperazin- 1- il)- ácido etanosulfonico {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	0.68	Ver ejemplo	(300 MHz, $CDCl_3$) δ 2.02 (s, 3H), 2.30 (m, 4H), 2.95 (m, 4H), 3.35 (m, 4H), 3.55 (m, 2H), 5.30 (d, 2H), 5.42 (s, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.35 (m, 5H), 8.00 (d, 1H), 10.17 (s, 1H)	580
I- 256		2- pirrolidin- 1- il- ácido etanosulfonico {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	0.23	Ver ejemplo	(300 MHz, $CDCl_3$) δ 1.60- 1.80 (m, 4H), 2.40- 2.55 (m, 4H), 3.02 (t, J = 6.6 Hz, 2H), 3.29 (t, J = 6.6 Hz, 2H), 5.08 (s, 2H), 5.29 (d, J = 1.3 Hz, 2H), 6.95- 7.05 (m, 1H), 7.10- 7.20 (m, 1H), 7.25- 7.45 (m, 5H), 7.97 (d, J = 1.7 Hz, 1 H)	524
I- 257		2- morfolin- 4- il- ácido etanosulfonico {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	1.64	Ver ejemplo	(300 MHz, $CDCl_3$) δ 2.42 (t, J = 4.6 Hz, 4H), 2.90 (t, J = 6.9 Hz, 2H), 3.31 (t, J = 6.9 Hz, 2H), 3.62 (t, J = 4.6 Hz, 4H), 5.24 (s, 2H), 5.30 (d, J = 1.3 Hz, 2H), 6.95- 7.05 (m, 1H), 7.10- 7.20 (m, 1H), 7.30- 7.45 (m, 5H), 7.99 (d, J = 1.6 Hz, 1H), 9.38 (s, 1H)	540

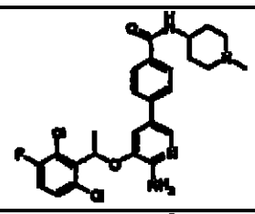
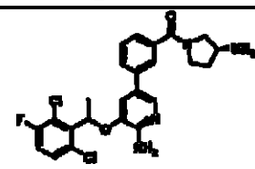
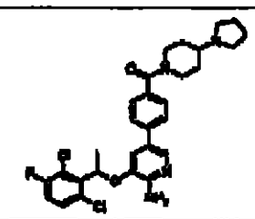
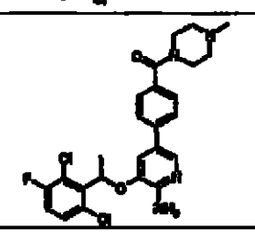
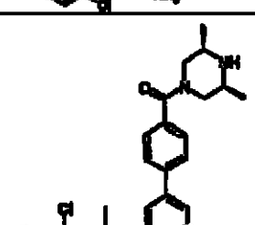
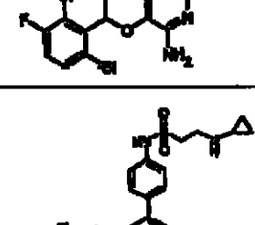
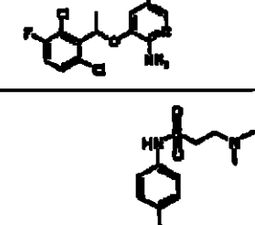
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 258		2- dietilamina- ácido etanosulfonico {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	1.67	Ver ejemplo	(300 MHz, $CDCl_3$) δ 1.00 (t, 6H), 2.52 (q, 4H), 3.02 (t, 2H), 3.25 (t,2H), 5.19 (s, 2H), 5.29 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.35 (m, 5H), 7.98 (d, 1H)	526
I- 259		2- dimetilamina- ácido etanosulfonico {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	1.5	Ver ejemplo	(300 MHz, $CDCl_3$) δ 2.24 (s, 6H), 2.85 (t, 2H), 3.24 (t, 2H), 5.11 (s, 2H), 5.29 (d, 2H), 7.07 (m, 1H), 7.15 (m, 1H), 7.35 (m, 5H), 7.98 (d, 1H)	498
I- 260		2- piperidin- 1- il- ácido etanosulfonico {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	1.63	Ver ejemplo	(300 MHz, $CDCl_3$) δ 1.30- 1.60 (m, 6H), 2.30- 2.45 (m, 4H), 2.89 (t, J = 6.7 Hz, 2H), 2.28 (t, J = 6.7 Hz, 2H), 5.13 (s, 2H), 5.29 (d, J = 1.4 Hz, 2H), 6.95- 7.05 (m, 1H), 7.15- 7.45 (m, 6H), 7.98 (d, J = 1.6 Hz, 1H)	538
I- 261		2- [(3R)- 3- hidroximetil- pirrolidin- 1- il] ácido etanosulfonico {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	1.7	Ver ejemplo	(300 MHz, $CDCl_3$) δ 1.60- 1.8 (m, 4H), 2.05- 2.15 (m, 1H), 2.55- 2.75 (m, 2H), 2.95- 3.15 (m, 2H), 3.25- 3.55 (m, 3H), 3.82 (dd, J = 3.0, 11.2 Hz, 1H), 4.97 (s, 2H), 5.28 (d, J = 1.6 Hz, 2H), 6.98- 7.08 (m, 1H), 7.10- 7.20 (m, 1H), 7.25- 7.45 (m, 5H), 7.98 (d, J = 1.8 Hz, 1H)	554
I- 262		2- (3- hidroxi- piperidin- 1- il) ácido etanosulfonico {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	1.5	Ver ejemplo	(300 MHz, DMSO- d_6) δ 1.15- 1.30 (m, 2H), 1.45- 1.55 (m, 2H), 1.90- 2.02 (m, 2H), 2.50- 2.70 (m, 4H), 4.49 (br s, 1H), 5.28 (s, 2H), 5.82 (s, 2H), 7.05- 7.10 (m, 1H), 7.20- 7.40 (m, 5H), 7.45- 7.60 (m, 1H), 7.83 (d, J = 1.6 Hz, 1H)	554
I- 263		2- [4- (2- hidroxi- acetil)piperazin- 1- il]- ácido etanosulfonico {3- [6- amino- 5- (2- cloro- 3,6- difluoro- bencíloxi)- piridin- 3- il]- fenil}- amida	1.14	Ver ejemplo	(300 MHz, $CDCl_3$) δ 2.36 (m, 4H), 2.92 (t, 2H), 3.14 (m, 2H), 3.32 (t, 2H), 3.54 (m, 2H), 3.60 (br s, 1H), 4.07 (s, 2H), 5.30 (s, 2H), 5.40 (br s, 2H), 7.06 (m, 1H), 7.24 (m, 2H), 7.34 (m, 2H), 7.44 (m, 2H), 7.99 (d, J = 1.6 Hz, 1H), 9.88 (br s, 1H)	596
I- 264		2- [(3R)- 3- hidroxi- pirrolidin- 1- il] ácido etanosulfonico {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	1.097	Ver ejemplo	(300 MHz, $CDCl_3$) δ 1.65 (m, 1H), 2.08 (m, 1H), 2.22 (m, 1H), 2.46 (m, 1H), 2.76 (m, 1H), 2.87 (m, 1H), 3.02 (m, 2H), 3.32 (m, 2H), 4.28 (m, 1H), 5.28 (br s, 2H) 5.29 (s, 2H), 7.06 (m, 1H), 7.24 (m, 2H), 7.44 (m, 5H), 8.00 (d, J = 1.7 Hz, 1H)	539

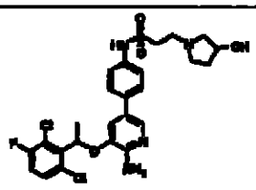
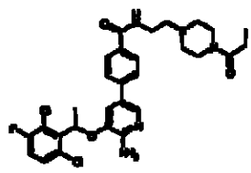
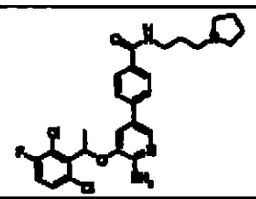
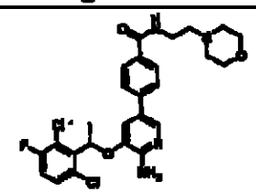
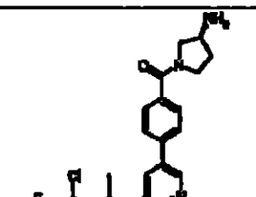
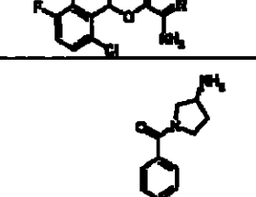
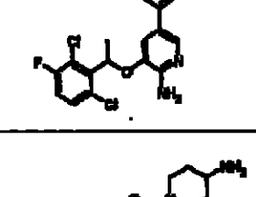
No.	Estructura	Nombre	Met IC_{20} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 265		2- (ciclopropilmetil- amino) ácido etanosulfonico {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	1	Ver ejemplo	(300 MHz, $CDCl_3$) δ 0.02 (m, 2H), 0.39 (m, 2H), 0.84 (m, 1H), 2.40 (d, 2H), 3.14 (t, 2H), 3.32 (t, 2H), 5.28 (s, 2H), 5.38 (br s, 2H), 7.06 (m, 1H), 7.24 (m, 2H), 7.44 (m, 5H), 8.00 (d, J = 1.7 Hz, 1H)	523
I- 266		2- (ciclopropilamino)- ácido etanosulfonico {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida	0.9	Ver ejemplo	(300 MHz, $CDCl_3$) δ 0.28 (m, 2H), 0.37 (m, 2H), 2.06 (m, 1H), 3.15- 3.40 (m, 4H), 5.30 (d, 2H), 5.39 (s, 2H), 7.07 (m, 1H), 7.19 (m, 1H), 7.30- 7.55 (m, 5H), 8.01 (d, 1H)	509
I- 267	 TFA	3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (2- dimetilaminometil- fenil)- piridin- 2- ilamina; compuesto con ácido trifluoro- acetico		Ver ejemplo		404
I- 268	 TFA	3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (2- pirrolidin- 1- il- fenil)- piridin- 2- ilamina; compuesto con ácido trifluoro- acetico	4	Ver ejemplo	(400 MHz, DMSO- d_6) δ 1.94 (t, 4H), 3.31 (t, 4H), 5.44 (s, 2H), 6.56 (d, 1H), 6.74 (s, 1H), 6.88 (d, 1H), 7.24 (t, 1H), 7.43 (m, 1H), 7.58 (m, 3H), 7.83 (m, 2H)	416
I- 269	 TFA	N- {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- metanosulfonamida; compuesto con ácido trifluoro- acetico		Ver ejemplo	(400 MHz, DMSO- d_6) δ 2.99 (s, 3H), 5.35 (s, 2H), 6.72 (br s, 2H), 7.27 (d, 2H), 7.42 (m, 1H), 7.59 (m, 1H), 7.65 (d, 2H), 7.73 (s, 1H), 7.84 (s, 1H), 9.79 (s, 1H)	440
I- 270		ácido 5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofeno- 2- carbolico		Ver ejemplo		397
I- 271		{5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofen- 2- il}- (4- metil- piperazin- 1- il)- metanona		Ver ejemplo	(300 MHz, $CDCl_3$) δ 8.00 (d, J = 1.8 Hz, 1H), 7.30 (d, J = 1.8 Hz, 1H), 7.25 (d, J = 1.5 Hz, 1H), 7.20 (m, 1H), 7.10 (d, J = 3.8 Hz, 1H), 7.07 (m, 1H), 5.27 (d, J = 1.7 Hz, 2H), 4.82 (br s, 2H), 3.81 (m, 4H), 2.47 (m, 4H), 2.34 (s, 3H)	479
I- 272		{5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofen- 2- il}- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona		Ver ejemplo	(300 MHz, $CDCl_3$) δ 8.02 (d, J = 1.8 Hz, 1H), 7.52 (m, 1H), 7.32 (d, J = 1.8 Hz, 1H), 7.21 (m, 1H), 7.14 (d, J = 3.9 Hz, 1H), 7.07 (m, 1H), 5.27 (d, J = 1.5 Hz, 2H), 4.80 (br s, 2H), 4.50 (m, 1H), 3.81 (m, 2H), 2.74 (m, 4H), 2.25- 1.82 (m, 10H).	533

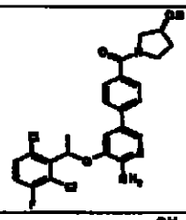
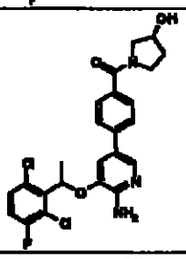
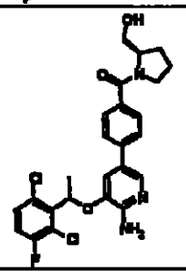
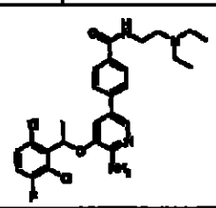
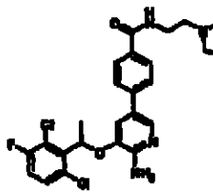
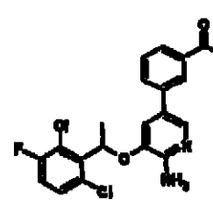
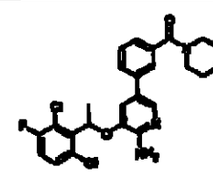
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 273		ácido 5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofeno- 2- carboxílico (1- metil- piperidin- 4- il)- amida		Ver ejemplo	(300 MHz, $CDCl_3$) δ 8.02 (d, J = 1.8 Hz, 1H), 7.42 (d, J = 3.9 Hz, 1H), 7.29 (d, J = 1.8 Hz, 1H), 7.21 (m, 1H), 7.15 (d, J = 3.9 Hz, 1H), 7.07 (m, 1H), 5.89 (br d, 1H), 5.29 (d, J = 1.5 Hz, 2H), 4.62 (br s, 2H), 4.05 (m, 1H), 3.05 (m, 2H), 2.50 (s, 3H), 2.40 (m, 2H), 1.85 (m, 2H), 1.62 (m, 2H)	493
I- 274		{5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofen- 2- il}- (3,5- dimetil- piperazin- 1- il)- metanona		Ver ejemplo	(300 MHz, $CDCl_3$) δ 8.00 (d, J = 1.8 Hz, 1H), 7.30 (d, J = 1.8 Hz, 1H), 7.24 (d, J = 3.8 Hz, 1H), 7.21 (m, 1H), 7.10 (d, J = 3.8 Hz, 1H), 7.07 (m, 1H), 5.28 (d, J = 1.5 Hz, 2H), 4.82 (br s, 2H), 4.38 (m, 2H), 2.98 (m, 2H), 2.65 (m, 2H), 1.68 (br s, 1H), 1.11 (d, J = 6.2 Hz, 6H)	493
I- 275		ácido 5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofeno- 2- carboxílico (2- pirrolidin- 1- il- etil)- amida		Ver ejemplo	(300 MHz, $CDCl_3$) δ 8.00 (d, J = 1.8 Hz, 1H), 7.82 (br m, 1H), 7.66 (d, J = 3.9 Hz, 1H), 7.29 (d, J = 1.8 Hz, 1H), 7.21 (m, 1H), 7.11 (d, J = 3.9 Hz, 1H), 7.07 (m, 1H), 5.26 (d, J = 1.5 Hz, 2H), 4.81 (br s, 2H), 3.71 (m, 2H), 3.02 (m, 2H), 2.95 (m, 2H), 2.01 (m, 4H), 1.97 (m, 2H), 1.11 (d, J = 6.2 Hz, 6H)	493
I- 276		{5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofen- 2- il}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona		Ver ejemplo	(300 MHz, $CDCl_3$) δ 6.00 (d, J = 1.8 Hz, 1H), 7.29 (d, J = 1.6 Hz, 1H), 7.24 (d, J = 3.8 Hz, 1H), 7.20 (m, 1H), 7.09 (d, J = 3.8 Hz, 1H), 7.07 (m, 1H), 5.27 (d, J = 1.5 Hz, 2H), 4.80 (br s, 2H), 4.43 (m, 2H), 3.10 (m, 2H), 2.63 (m, 4H), 2.34 (m, 1H), 1.99 (m, 2H), 1.83 (m, 4H), 1.63 (m, 2H).	533
I- 277		ácido 4- [6- amino- 5- (3- fluro- 2- trifluorometil- benciloxi)- piridin- 3- il]- benzoico		Ver ejemplo		407
I- 278		{4- [6- amino- 5- (3- fluro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il]- metanona		Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.97 (d, J = 1.8 Hz, 1H), 7.61- 7.42 (m, 6H), 7.21 (d, J = 8.7 Hz, 1H), 7.12 (d, J = 1.8 Hz, 1H), 5.33 (s, 2H), 4.81 (br s, 2H), 4.62 (m, 1H), 3.84 (m, 1H), 2.98 (m, 2H), 2.65 (m, 4H), 2.32 (m, 1H), 1.97 (m, 2H), 1.84 (m, 4H) 1.60 (m, 2H)	543

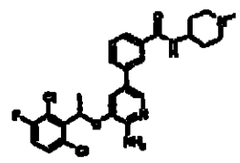
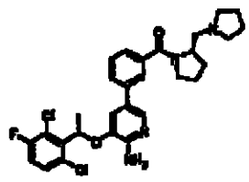
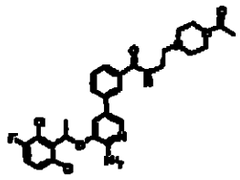
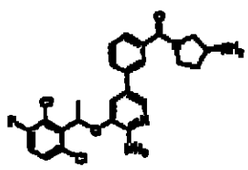
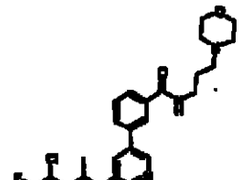
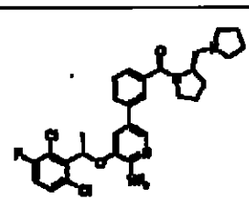
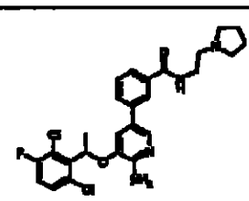
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 279		4- [6- amino- 5- (3- fluro- 2- trifluorometil- benciloxi)- piridin- 3- il]- N- (1- metil- piperidin- 4- il]- benzamida		Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.99 (d, J 1.8 Hz, 1H), 7.80 (d, J = 8.3 Hz, 2H), 7.55 (m, 1 H), 7.52 (d, J = 8.3 Hz, 2H>, 7.44 (d. J 7.8 Hz, 1H), 7.22 (I, = 8.7 Hz, 1H), 7.12 (d, J = 1.8 Hz, 1H), 5.99 (br d, 1 R), 5.34 (s, 2H), 4.83 (br s, 2H), 4.04 (m, 1 H), 2.87 (m, 21- 1), 2.34 (s, OH), 2.20 (m, 2H), 2.05 (m. 2H), 1.63 (m, 2H)	503
I- 280		[4- [6- amino- 5- (3- fluro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il]- metanona		Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.98 (s, 1 H), 7.61- 7.43 (m, 6H), 7.22 (t, J = 8.7 Hz, 1H), 7.13 (d, J = 1.6 Hz, 1H), 5.33 (s, 2H), 4.82 (br s, 2H), 4.65 (m, 1H), 3.65 (m. 1H), 2.90 (m, 2H), 2.68 (m, 1H). 2.42 (m, 1H), 1.60 (m. 1H), 1.12 (d, 3H), 1.00 (d, 3H)	503
I- 281		[4- [6- amino- 5- (3- fluro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (3- dimetilamino- pirrolidin- 1- il}- metanona		Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.98 (d, J = 2.4 Hz, 1H), 7.61- 7.43 (m, 6H), 7.21 (t, J = 8.8 Hz, 1H), 7.14 (d, J = 2.4 Hz, 1H), 5.33 (s, 2H). 4.87 (br s, 2H), 3.89 (m, 1H), 3.65 (m, 2H), 3.42 (m, 1H), 2.70 1.02 (m, 1H), 2.32 (s, 3H), 2.23 (s, 3H), 2.14 (m, 1H), 1.82 (m, 1H),	503
I- 282		[4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil]- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona		Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.98 (d, J = 1.4 Hz, 1H), 7.58- 7.43 (m, 6H), 7.20 (t, J = 8.8 Hz, 1H), 7.13 (d, J = 1.4 Hz, 1H), 5.34 (s, 2H), 4.81 (br s, 2H), 4.46 (m, 1H), 7.50 (m, 2H), 2.77 (m, 4H), 2.30- 1.50 (m, 10H)	543
I- 283		4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- #N!- (2- morfolin- 4- il- etil)- benzamida		Ver ejemplo	(300 MHz, $CDCl_3$) δ 8.00 (d, J = 1.2 Hz, 1H), 7.83 (d, J = 8.2 Hz, 2H), 7.56 (m, 1H), 7.55 (d, J = 8.2 Hz, 2H), 7.45 (d, 1H), 7.20 (t, J = 8.8 Hz, 1H), 7.13 (d, J = 1.4 Hz, 1H), 6.76 (m, 1H), 5.34 (s, 2H), 4.85 (br s, 2H), 3.74 (m, 4H), 3.56 (m, 2H), 2.62 (m, 2H), 2.52 (m, 4H)	519
I- 284		[4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il]- metanona		Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.97 (d, J = 1.8 Hz, 1H). 7.58- 7.43 (m, 6H), 7.20 (t, J = 8.8 Hz, 1H), 7.12 (d, J = 1.8 Hz, 1H), 5.34 (s, 2H), 4.93 (br s, 2H), 3.80 (m, 2H), 3.56 (m, 2H), 2.44 (m, 4H), 2.33 (s, 3H)	489

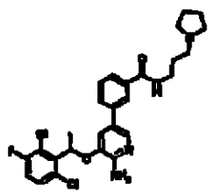
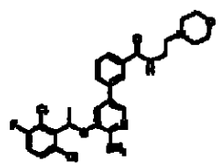
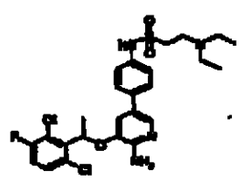
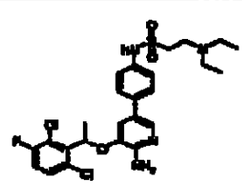
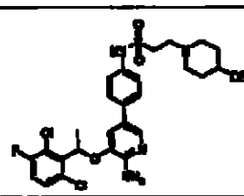
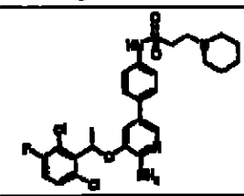
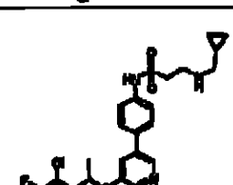
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 285		N- [2- (4- acetil- piperazin- 1- il)- etil]- 4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- benzamida		Ver ejemplo	(300 MHz, $CDCl_3$) δ 8.00 (d, J = 1.2 Hz, 1H), 7.82 (d, J = 8.2 Hz, 2H), 7.58 (m, 1H), 7.55 (d, J = 8.2 Hz, 2H), 7.44 (d, J = 7.8 Hz, 1H), 7.22 (t, J = 8.8 Hz, 1H), 7.14 (d, J = 1.4 Hz, 1H), 6.72 (m, 1H), 5.34 (s, 2H), 4.85 (br s, 2H), 3.65 (m, 2H), 3.60 (m, 2H), 3.50 (m, 2H), 2.65 (m, 2H), 2.51 (m, 4H), 2.10 (s, 3H)	560
I- 286		2- piperidin- 1- il- ácido etanosulfonico (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0.18	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.26 (d, 2H), 7.20 (d, 2H), 7.06 (m, 3H), 7.59 (s, 1H), 4.86 (s, 2H), 3.25 (m, 2H), 2.89 (m, 2H), 2.49 (m, 4H), 1.83 (d, 3H), 1.62 (m, 4H), 1.48 (m, 2H)	551
I- 287		2- (4- hidroxi- piperidin- 1- il)- ácido etanosulfonico (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0.14	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.26 (d, 2H), 7.20 (d, 2H), 7.06 (m, 3H), 7.59 (s, 1H), 4.86 (s, 2H), 3.76 (m, 1H), 3.25 (m, 2H), 2.89 (m, 2H), 2.78 (m, 2H), 2.26 (m, 2H), 1.83 (m, 5H), 1.62 (m, 2H)	567
I- 288		2- dimetilamino- ácido etanosulfonico (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0.15	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.26 (d, 2H), 7.20 (d, 2H), 7.06 (m, 3H), 7.59 (s, 1H), 4.86 (s, 2H), 3.21 (m, 2H), 2.88 (m, 2H), 2.30 (s, 6H), 2.26 (m, 2H), 1.82 (d, 3H)	511
I- 289		2- ciclopropilamino- ácido etanosulfonico (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0.16	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.38 (d, 2H), 7.26 (d, 2H), 7.18 (m, 3H), 5.95 (m, 1H), 4.89 (s, 2H), 3.22 (m, 4H), 2.14 (m, 1H), 1.85 (d, 3H), 0.50 (m, 2H), 0.38 (m, 2H)	523
I- 290		ácido 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluro- 2- fenil)- etoxi]- piridin- 3- il}- benzoico		Ver ejemplo		422
I- 291		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- [(2H)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.063	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.52 (d, 2H), 7.31 (d, 2H), 7.08 (m, 3H), 6.13 (m, 1H), 4.86 (s, 2H), 4.30 (m, 1H), 3.40 (m, 2H), 2.60 (m, 4H), 1.82 (d, 3H), 1.70- 2.0 (m, 10H)	557

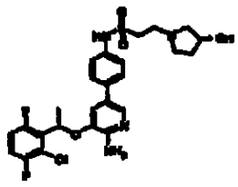
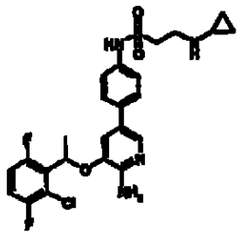
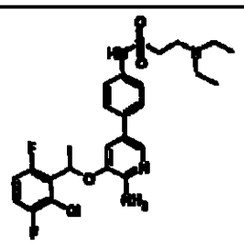
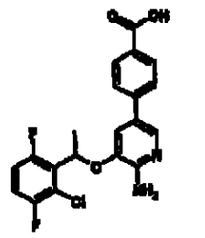
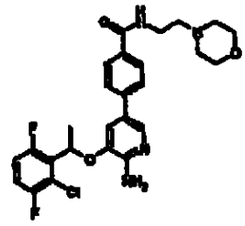
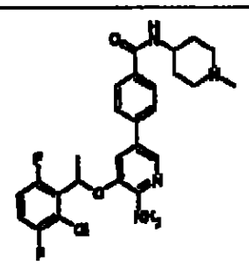
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^1H- NMR	MS m/z (M+1)
I- 292		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (1- metil- piperidin- 4- il)- benzamida	0.069	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.78 (d, 2H), 7.35 (d, 2H), 7.31 (m, 3H), 6.16 (sxt, 1H), 5.90 (d, 1H), 4.86 (s, 2H), 4.05 (m, 1H), 2.85 (d, 1H), 2.35 (s, 3H), 2.05 (d, 1H), 2.25 (t, 1H), 1.82 (d, 3H), 1.60 (m, 1H), 1.29 (m, 2H), 0.86 (m, 2H)	559
I- 293		(3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- [(3R)- 3- amino- pirrolidin- 1- il)]- metanona	0.051	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.51 (s, 1H), 7.38 (m, 3H), 7.30 (m, 1H), 7.15 (m, 1H), 6.97 (s, 1H), 6.15 (m, 1H), 4.94 (s, 2H), 3.45- 3.89 (m, 4H), 3.20 (m, 1H), 2.25 (m, 1H), 2.15 (m, 1H), 1.82 (d, 3H), 1.34 (m, 2H)	489
I- 294		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piridin- 3- il)- metanona	0.062	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.70 (m, 1 H) 7.45 (m, 1H), 7.30 (s, 2H), 7.08 (t, 1H), 6.92 (d, 2H), 6.13 (m, 1H), 4.86 (s, 2H), 4.30 (t, 1H), 2.80 (m, 4H), 1.82 (d, 3H), 1.80 (m, 4H), 1.35 (m. 4H), 0.89 (m, 4H)	559
I- 295		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona	0.079	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.71 (d, 2H), 7.49 (d, 2H), 7.40 (s, 1H), 7.35 (m, 1H), 7.08 (m, 1H), 6.17 (m, 1H), 4.98 (s, 2H), 4.28 (t, 2H), 3.68 (m, 4H), 2.38 (m, 2H), 2.31 (s, 3H), 1.88 (d, 3H)	503
I- 296		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (3,5- dimetil- piperazi- 1- il)- metanona	0.054	Ver ejemplo		
I- 297		2- ciclopropilamino- ácido etanosulfonico (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0.164	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.30 (m, 3H), 7.24 (m, 3H), 7.08 (t, 1H), 6.95 (s, 1H), 6.09 (m, 1H), 4.89 (s, 2H), 3.21 (m, 4H), 2.12 (m, 1H), 1.84 (d, 3H), 0.87 (m, 1H), 0.50 (m, 2H), 0.36 (m, 2H)	539
I- 298		2- dimetilamino- ácido etanosulfonico (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0.059	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.26 (m, 6H), 7.04 (t, 1H), 6.94 (s, 1H), 6.12 (m, 1H), 4.95 (s, 2H), 3.21 (t, 2H), 2.85 (t, 2H). 2.31 (s, 6H), 1.85 (d, 3H)	527

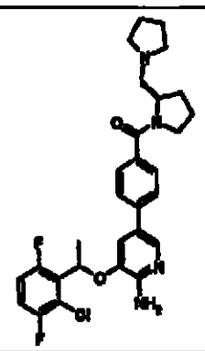
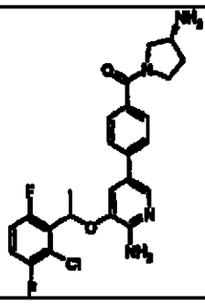
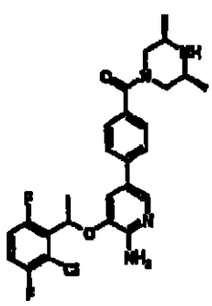
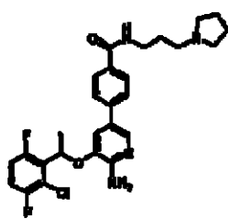
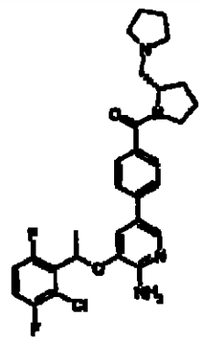
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^1H- NMR	MS m/z (M+1)
I- 299		2- [(3R)- 3- hidroxi- pirrolidin- 1- il)]- ácido etanosulfónico (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0.062	Ver ejemplo	(300 MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.30 (m, 5H), 7.10 (t, 1H), 6.89 (s, 1H), 6.10 (tert, 1H), 4.86 (s, 2H), 4.40 (s, 1H), 3.21 (m, 2H), 2.88 (m, 3H), 2.67 (d, 1H), 2.46 (m, 1H), 2.20 (m, 2H), 2.05 (s, 1H), 1.85 (d, 3H), 1.25 (s, 1H)	570
I- 300		N- [2- (4- acetil- piperazin- 1- il) etil]- 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- benzamida	0.059		(300 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.79 (d, 2H), 7.42 (d, 2H), 7.30 (dd, 1H), 7.07 (t, 1H), 7.02 (d, 1H), 6.81 (bm, 1H), 6.13 (q, 1H), 5.42 (s, 2H), 3.80 (m, 2H), 3.62 (m, 2H), 3.53 (m, 2H), 2.68 (m, 2H), 2.52 (m, 4H), 2.10 (s, 3H), 1.87 (d, 3H).	575 [M+1]
I- 301		4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il)- N- (3- pirrolidin- 1- il- propil)- benzamida	0.064		(300 MHz, $CDCl_3$) δ 8.71 (bm, 1H), 7.92 (m, 3H), 7.42 (d, 2H) 7.31 (dd, 1H), 7.06 (t, 1H), 7.01 (s, 1H), 6.12 (q, 1H), 4.97 (s, 2H), 3.65 (m, 2H), 3.00 (m, 6H), 2.00 (m, 6H), 1.87 (d, 3H).	533 [M+1]
I- 302		4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il)- N- (2- morfolin- 4- il- etil) benzamida	0.071		(300 MHz, $CDCl_3$) δ 7.90 (d, 1H), 7.79 (d, 2H), 7.44 (d, 2H), 7.31 (dd, 1H), 7.06 (t, 1H), 7.01 (d, 1H), 6.83 (bm, 1H), 6.12 (q, 1H), 5.05 (s, 2H), 3.74 (m, 4H), 3.58 (m, 2H), 2.63 (m, 2H), 2.53 (m, 4H) 1.87 (d, 3H).	533 [M+1]
I- 303		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 3- amino- pirrolidin- 1- il)- metanona	0.059		(300 MHz, CD_3OD) δ 7.76 (s, 1H), 7.54 (m, 1H), 7.42 (m, 4H), 7.24 (t, 1H), 7.04 (s, 1H), 6.22 (q, 1H), 4.82 (s, 2H), 3.76 (m, 1H), 3.68 (m, 2H), 3.52 (m, 1H), 2.28 (m, 1H), 1.92 (m, 3H), 1.75 (m, 1H), 1.42 (m, 1H),	491 [M+1]
I- 304		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona	0.072		(300 MHz, CD_3OD) δ 7.76 (s, 1H), 7.54 (m, 1H), 7.42 (m, 4H), 7.24 (t, 1H), 7.04 (s, 1H), 6.22 (q, 1H), 4.82 (s, 2H), 3.76 (m, 1H), 3.68 (m, 2H), 3.52 (m, 1H), 2.28 (m, 1H), 1.92 (m, 3H), 1.75 (m, 1H), 1.42 (m, 1H).	491 [M+1]
I- 305		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- amino- piperidin- 1- il)- metanona	0.18			504 [M+1]

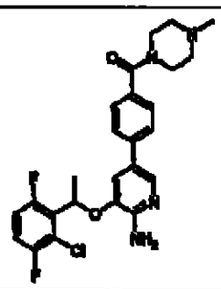
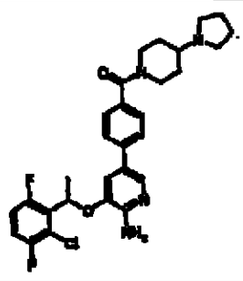
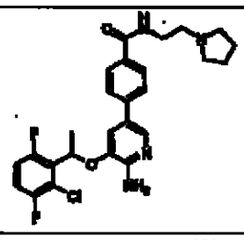
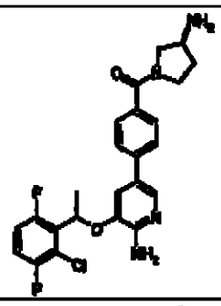
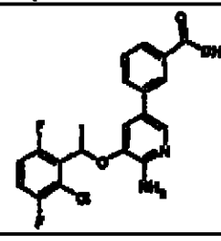
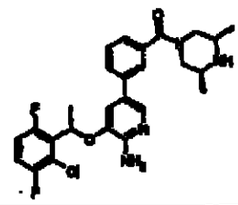
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 306		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 3- hidroxi- pirrolidin- 1- il)- metanona	0.024		(300 MHz, CD_3OD) δ 7.78 (d, 1H), 7.47 (m, 3H), 7.37 (m, 3H), 6.92 (d, 1H), 6.07 (q, 1H), 5,88 (s, 2H), 4.82 (dd, 1H), 4.15 (d, 1H), 3.53 (m, 2H), 3.42 (m, 1H), 3.15 (m, 1H), 2.43 (m, 1H), 1.85 (m, 1H), 1.75 (d, 3H).	491 [M+1]
I- 307		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 3- hidroxi- pirrolidin- 1- il)- metanona	0.022		(300 MHz, CD_3OD) δ 7.80 (d, 1H), 7.47 (m, 3H), 7.37 (m, 3H), 6.92 (d, 1H), 6.07 (q, 1H), 5.89 (s, 2H), 4.82 (dd, 1H), 4.15 (d, 1H), 3.53 (m, 2H), 3.42 (m, 1H), 3.15 (m, 1H), 2.43 (m, 1H), 1.85 (m, 1H), 1.75 (d, 3H).	491 [M+1]
I- 308		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 3- hidroximetil- pirrolidin- 1- il)- metanona	0.033		(300 MHz, CD_3OD) δ 7.80 (d, 1H), 7.47 (m, 3H), 7.37 (m, 3H), 6.92 (d, 1H), 6.07 (q, 1H), 5.89 (s, 2H), 4.70 (m, 1H), 4.05 (m, 1H), 3.5 (m, 2H), 3.32 (m, 1H), 2.43 (m, 1H), 1.85 (m, 3H), 1.75 (d, 3H), 1.15 (m, 1H).	505 [M+1]
I- 309	 TFA	4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- dietilamino- etil)- benzamida	0.04		(300 MHz, $CDCl_3$) δ 9.55 (bm 1H), 8.80 (t, 1H), 7.95 (s, 1H), 7.58 (d, 2H), 7.55 (m, 3H), 7.45 (t, 1H), 7.09 (d, 1H), 6.23 (q, 1H), 3.60 (q, 2H), 3.22 (m, 5H), 3.09 (m, 1H), 1.85 (d, 3H), 1.22 (dd, 6H)	519 [M+1]
I- 310		4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida	0.12		(300 MHz, $CDCl_3$) δ 8.25 (bm, 1H), 7.90 (d, 1H), 7.82 (s, 2H), 7.34 (d, 2H), 7.25 (m, 1H), 7.04 (t, 1H), 6.96 (s, 1H), 6.09 (q, 1H), 4.97 (s, 2H), 3.82 (m, 2H), 3.15 (m, 6H), 2.00 (m, 4H), 1.85 (d, 3H).	518 [M+1]
I- 311		ácido 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- benzoico				420 [M- 1]
I- 312		(3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona	0.062		(300 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.41 (m, 3H), 7.30 (m, 3H), 7.07 (t, 1H), 6.99 (s, 1H), 6.12 (q, 1H), 4.99 (s, 2H), 3.89 (m, 2H), 3.50 (m, 2H), 2.54 (m, 2H), 2.40 (m, 2H), 2.35 (s, 3H), 1.87 (d, 3H).	503 [M+1]

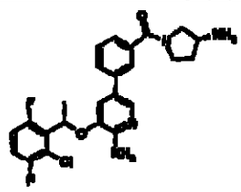
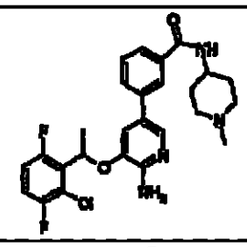
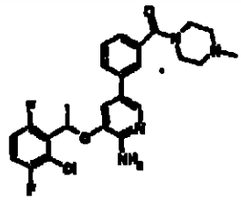
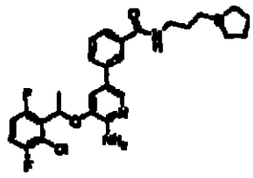
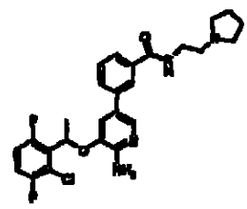
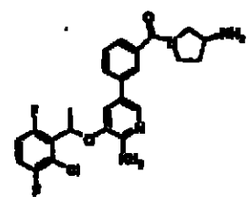
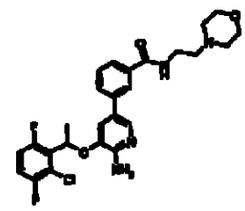
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I-313		3-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-N-(1-metil-piperidin-4-il)-benzamida	0.069		(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.76 (s, 1H), 7.67 (d, 1H), 7.49 (d, 1H), 7.42 (t, 1H), 7.31 (dd, 1H), 7.05 (t, 1H), 7.01 (s, 1H), 6.28 (bd, 1H), 6.12 (q, 1H), 4.99 (s, 2H), 4.08 (m, 1H), 3,04 (m, 2H), 2.42 (s, 3H), 2.32 (m, 2H), 2.10 (m, 2H), 1.87 (d, 3H), 1.80 (m, 2H).	517 [M+1]
I-314		(3-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-fenil)-((S)-2-pirrolidin-1-ilmetil-pirrolidin-1-il)-metanona	0.06		(300 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.40 (m, 4H), 7.29 (dd, 1H), 7.05 (t, 1H), 7.00 (s, 1H), 6.12 (q, 1H), 4.92 (s, 2H), 3.50 (m, 2H), 3.74 (m, 4H), 1.86 (d, 3H), 1.57-2.18 (m, 11H).	559 [M+1]
I-315		N-{2-(4-acetil-piperazin-1-il) etil}-3-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-benzamida	0.069		(300 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.83 (s, 1H), 7.65 (d, 1H), 7.46 (m, 2H), 7.32 (dd, 1H), 7.06 (t, 1H), 7.03 (s, 1H), 6.95 (bt, 1H), 6.12 (q, 1H), 5.08 (s, 2H), 3.66 (m, 4H), 3.50 (m, 2H), 2.73 (m, 2H), 2.52 (m, 4H), 2.09 (s, 3H), 1.87 (d, 3H).	576 [M+1]
I-316		(3-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-fenil)-((S)-3-amino-pirrolidin-1-il)-metanona	0.048		(300 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.38 (m, 4H), 7.28 (m, 1H), 7.06 (t, 1H), 6.98 (s, 1H), 6.12 (q, 1H), 5.05 (s, 2H), 3.82 (m, 2H), 3.72 (m, 2H), 2.10 (m, 1H), 1.86 (d, 3H), 1.84 (m, 2H).	491 [M+1]
I-317		3-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-N-(3-morfolin-4-il-prupil)benzamida	0.059		(300 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.87 (s, 1H), 7.85 (d, 1H), 7.50 (m, 2H), 7.31 (dd, 1H), 7.04 (m, 2H), 6.13 (q, 1H), 4.93 (s, 2H), 3.64 (m, 6H), 2.50 (m, 6H), 1.87 (d, 3H), 1.81 (m, 2H).	549 [M+1]
I-318		(3-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-fenil)-((R)-2-pirrolidin-1-ilmetil-pirrolidin-1-il)-metanona	0.13		(300 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.40 (m, 4H), 7.29 (dd, 1H), 7.05 (t, 1H), 7.00 (s, 1H), 6.12 (q, 1H), 4.92 (s, 2H), 3.50 (m, 2H), 3.74 (m, 4H), 1.86 (d, 3H), 1.57-2.18 (m, 11H).	558 [M+1]
I-319		3-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-N-(2-pirrolidin-1-il-etil)-benzamida	0.1		(300 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.82 (s, 1H), 7.73 (d, 1H), 7.46 (m, 4H), 7.22 (t, 1H), 7.04 (s, 1H), 6.95 (bt, 1H), 6.22 (q, 1H), 4.82 (s, 2H), 3.60 (m, 2H), 2.82 (m, 2H), 2.70 (m, 4H), 1.87 (d, 3H), 1.82 (m, 2H).	518 [M+1]

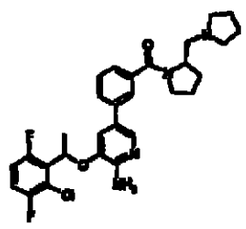
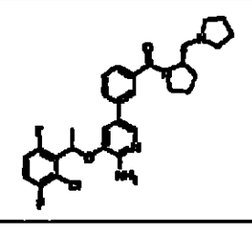
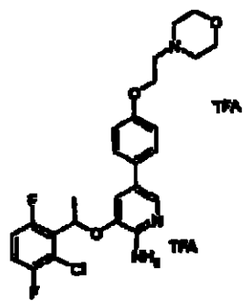
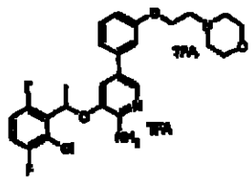
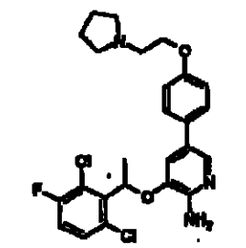
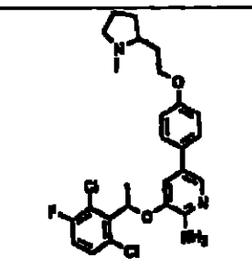
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 320		3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (3- pirrolidin- 1- il- propil)- benzamida	0.13		(300 MHz, $CDCl_3$) δ 8.66 (bt, 1H), 7.90 (s, 1H), 7.85 (s, 1H), 7,61 (d, 1H), 7.42 (m, 2H), 7.31 (dd, 1H), 7.05 (m, 2H), 6.14 (q, 1H), 4.88 (s, 2H), 3.65 (m, 2H), 2.71 (m, 2H), 2.56 (m. 4H). 1.87 (d, 3H), 1.80 (m, 2H), 1.71 (m, 4H).	531 [M+1]
I- 321		3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida	0.18		(300 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.84 (s, 1H), 7,66 (d, 1H), 7.46 (m, 2H), 7.32 (dd, 1H), 7.05 (m, 2H), 6.88 (bt, 1H), 6.14 (q, 1H), 5.04 (s, 2H), 3.82 (m, 4H), 3.66 (m, 2H), 2.72 (t, 2H), 2.60 (m, 4H), 1.88 (d, 3H),	535 [M+1]
I- 322		(3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- pirrolidin- 1- il)- metanona	0,071		(300 MHz, $CDCl_3$) δ 7.86 (s, 1H). 7.41 (m, 3H), 7.30 (m, 3H). 7.07 (t, 1H). 6.99 (s, 1H), 6.12 (q, 1H), 4.95 (s, 2H), 4.70 (m, 1H), 3.82 (m, 1H), 3.06 (m, 1H), 2.98 (m, 1H), 2.65 (m, 4H), 2.28 (m, 1H), 1.02 (m, 1H), 1.81 (m, 5H), 1.55 (m, 2H).	599 [M+1]
I- 323		2- dietilamina- ácido etanosulfonico (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0,08		(300 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.32 (m, 4H), 7.21 (d, 2H), 7.06 (t, 1H), 6.96 (s, 1H), 5.96 (q, 1H), 4.81 (s, 2H), 3.22 (m, 2H), 3.02 (m, 2H), 2.62 (m, 4H), 1.84 (d, 3H) 1.08 (t, 6H).	571 [M+1]
I- 324		2- (4- hidroxi- piperidin- 1- il)- ácido etanosulfonico (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0,059		(300 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.31 (m, 3H), 7.25 (m, 3H), 7.07 (t, 1H), 6.96 (s, 1H), 6.11 (q, 1H), 4.95 (s, 2H), 3.76 (m, 1H), 3.25 (t, 2H), 2.92 (t, 2H), 2.79 (m, 2H), 2.25 (m, 2H), 1.93 (m, 2H), 1.86 (d, 3H), 1.62 (m, 2H).	583 [M+1]
I- 325		2- piperidin- 1- il- ácido etanosulfonico (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0,089		(300 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.32 (m, 4H), 7.21 (d, 2H); 7.06 (dd, 1H), 6.96 (s, 1H), 6.11 (q, 1H), 4.88 (s, 2H), 3.24 (t, 2H), 2.89 (t, 2H), 2.48 (m, 4H), 1.86 (d, 3H). 1.62 (m, 4H), 1.49 (m, 2H).	558 [M+1]
I- 326		2- (Ciclopropilmetil- amino)- ácido etanosulfonico (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0,075		(300 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.28 (m, 6H), 7.06 (dd, 1H), 6.96 (s, 1H), 6.11 (q, 1H), 4.91 (s, 2H), 3.22 (m, 4H), 2.50 (d, 2H), 1.86 (d, 3H), 0.84 (m 2H), 0.52 (m, 2H), 0.15 (m, 1H).	517 [M+1]

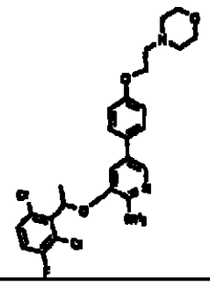
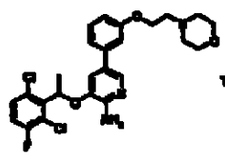
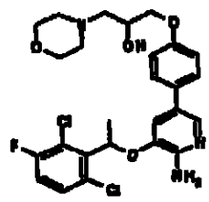
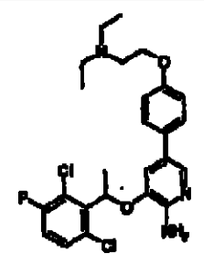
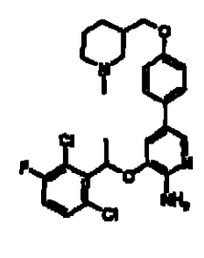
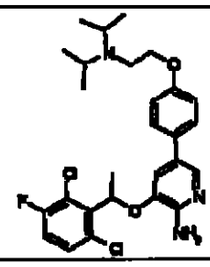
No.	Estructura	Nombre	Met IC_{20} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 327		2- ((R)- 3- hidroxi- pirrolidin- 1- il)- ácido etanosulfonico (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0.093		(300 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.32 (m, 5H), 7.05 (m, 3H), 5.95 (q, 1H), 4.84 (s, 2H), 4.43 (m, 1H), 3.25 (m, 2H), 3.02 (m, 3H), 2.84 (m, 1H), 2.53 (m, 1H), 2.30 (m, 1H), 2.22 (m, 1H), 1.84 (d, 3H), 1.81 (m, 1H).	553 [M+1]
I- 328		2- ciclopropilamino- ácido etanosulfonico (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0.16		(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.38 (d, 2H), 7.24 (m, 2H), 7.18 (m, 3H), 5.95 (q, 1H), 4.89 (s, 2H), 3.22 (m, 4H), 2.14 (m, 1H), 1.85 (d, 3H), 0.90 (m, 2H), 0.38 (m, 2H).	523 [M+1]
I- 329		2- dietilamino- ácido etanosulfonico (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0.095		(300 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.34 (d, 2H), 7.23 (m, 3H), 7.02 (m, 3H), 5.96 (q, 1H), 4.81 (s, 2H), 3.22 (m, 2H), 3.02 (m 2H), 2.62 (m, 4H), 1.84 (d, 3H), 1.08 (t, 6H).	539 [M+1]
I- 330		ácido 4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- benzoico				405 [M+1]
I- 331		4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida	0.13		(300 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.80 (d, 2H), 7.46 (d, 2H), 7.05 (m, 3H), 6.87 (m, 1H), 5.97 (q, 1H), 4.97 (s, 2H), 3.75 (m, 4H), 3.58 (m, 2H), 2.60 (m, 6H), 1.84 (m, 3H).	517 [M+1]
I- 332		4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (1- metil- piperidin- 4- il)- benzamida	0.079		(300 MHz, $CDCl_3$) δ 7,90 (s, 1H), 7.78 (d, 2H), 7.45 (d, 2H), 7.05 (m, 4H), 5.98 (q, 1H), 4.90 (s, 2H), 4.00 (m, 1H), 2.88 (m, 2H), 2.32 (s, 3H), 2.18 (m, 2H), 2.08 (m, 2H), 1.84 (d, 3H), 1.57 (m, 2H).	501 [M+1]

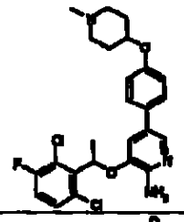
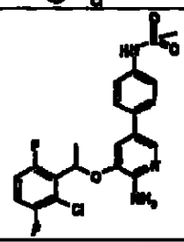
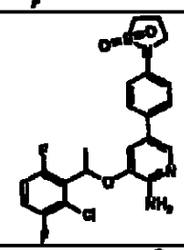
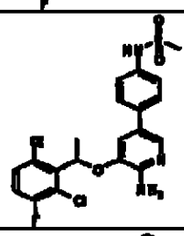
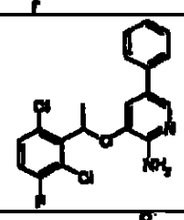
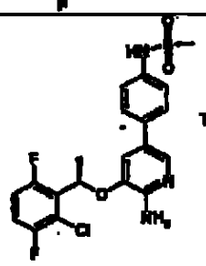
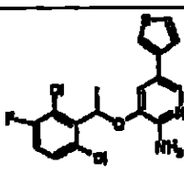
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 333		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.067		(300 MHz, $CDCl_3$) δ 7. 90 (s, 1H), 7.54 (m, 2H), 7.42 (d, 2H), 7.05 (m, 3H), 5.98 (q, 1H), 4.86 (s, 2H), 3,50 (m, 2H), 3.74 (m, 4H), 1.84 (d, 3H), 157- 2.18 (m, 11H)	541 [M+1]
I- 334		(4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona	0.089		(300 MHz, $CDCl_3$) δ 7.68 (m, 5H), 7.25 (m, 3H), 6.27 (m, 1H), 4.88 (s, 2H), 3.75 (m, 5H), 3.31 (m, 2H), 2.44 (m, 1H), 2.17 (m, 1H), 1.93 (m, 3H).	473 [M+1]
I- 335		(4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R,5S)- 3,5- dimetil- piperazin- 1- il)- metanona	0.09		(300 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.42 (m, 4H), 7.05 (m, 3H). 5.97 (q, 1H), 4.86 (s, 2H), 4.62 (m, 1H), 3.65 (m, 1H), 2.88 (m, 2H), 2.68 (m, 1H), 2.41 (m, 1H), 1.84 (d, 3H), 1.64 (m, 1H), 1.05 (m. 6H).	501 [M+1]
I- 336		4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (3- pirrolidin- 1- il- propil)- benzamida	0.09		(300 MHz, $CDCl_3$) δ 9.00 (s, 1H), 7.92 (s, 1H), 7.83 (d, 2H), 7.42 (d, 2H), 7.09 (m, 2H), 7.01 (m, 1H), 5.96 (q, 1H), 4.89 (s, 2H), 3.60 (m, 2H), 2.75 (m, 2H), 2.62 (m, 4H), 1.85 (m, 7H).	515 [M+1]
I- 337		(4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.09		(300 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.53 (m, 2H), 7.43 (d, 2H), 7.05 (m, 3H), 5.98 (q, 1H), 4.86 (s, 2H), 4.45 (m, 1H), 3.58 (m, 2H), 3.00 (m, 4H), 1.84 (d, 3H). 1.70- 2.18 (m, 10H)	541 [M+1]

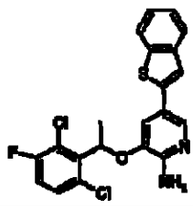
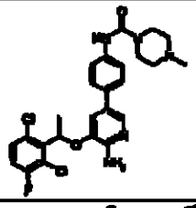
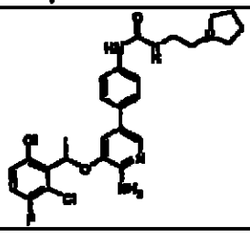
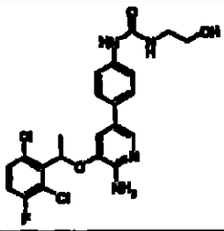
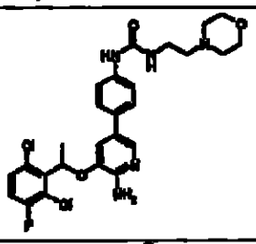
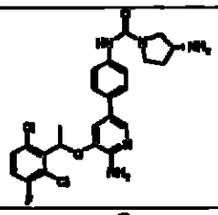
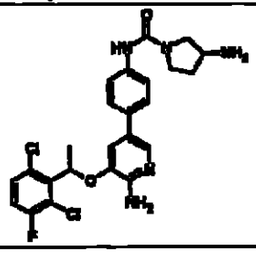
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 338		(4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona	0.077		(300 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.44 (m, 4H), 7.07 (m, 3H), 5.95 (q, 1H), 4.87 (s, 2H), 3.60 (m, 4H), 2.43 (m, 4H), 2.3 (s, 3H), 1.84 (d, 3H).	487 [M+1]
I- 339		(4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	0.062		(300 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.42 (m, 4H), 7.02 (m, 3H), 6.00 (q, 1H), 4.87 (s, 2H), 4.64 (m, 1H), 3.85 (m, 1H), 2.99 (m, 2H), 2.67 (m, 4H), 2.38 (m, 1H), 1.90 (m, 9H), 1.62 (m, 2H).	541 [M+1]
I- 340		4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida	0.086		(300 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.86 (d, 2H), 7.45 (d, 2H), 7.10 (m, 3H), 7.01 (m, 1H), 5.98 (q, 1H), 4.90 (s, 2H), 3.60 (m, 2H), 2.80 (m, 2H), 2.68 (m, 4H), 1.85 (m, 7H).	501 [M+1]
I- 341		(4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 3- amino- pirrolidin- 1- il)- metanona	0.075		(300 MHz, $CDCl_3$) δ 7.76 (s 1H), 7.67 (m, 2H), 7.59 (d, 2H), 7.42 (s, 1H), 7.32 (m, 1H), 7.20 (m, 1H), 6.27 (m, 1H), 4.86 (s, 2H), 3.75 (m, 5H), 3.31 (m, 2H), 2.44 (m, 1H), 2.14 (m, 1H), 1.95 (m, 3H).	473 [M+1]
I- 342		ácido 3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- benzoico				405 [M+1]
I- 343		(3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3S, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona	0.16		(300 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.43 (m, 2H), 7.30 (m, 2H) 7.10 (m, 2H), 6.95 (m, 1H), 5.97 (q, 1H), 4.87 (s, 2H), 4.65 (m, 1H), 3.60 (m, 1H), 2.72 (m, 3H), 2.41 (m, 1H), 2.01 (s, 1H), 1.84 (d, 3H), 1.17 (m, 3H), 0.98 (m, 3H).	501 [M+1]

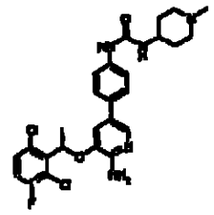
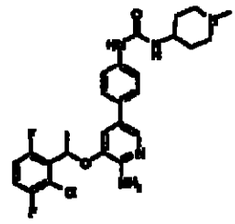
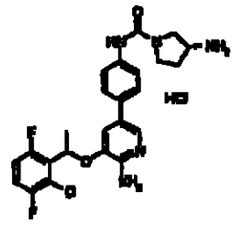
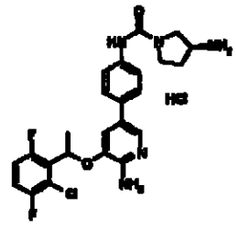
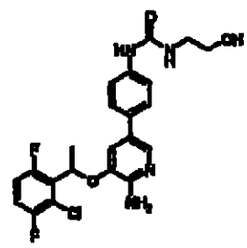
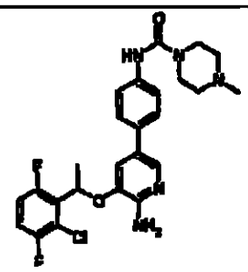
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 344		(3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona	0.12		(300 MHz, $CDCl_3$) δ 7.65 (m, 5H), 7.42 (s, 1H), 7.32 (m, 1H), 7.20 (m, 1H), 6.27 (m, 1H), 4.85 (s, 2H), 3.75 (m, 5H), 3.31 (m, 2H), 2.44 (m, 1H), 2.16 (m, 1H), 1.93 (m, 3H).	473 [M+1]
I- 345		3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (1- metil- piperidin- 4- il)- benzamida	0.2		(300 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.78 (s, 1H), 7.67 (d, 1H) 7.45 (m, 2H), 7.00 (m, 3H), 6.15 (bd, 1H), 5.98 (q, 1H), 4.08 (m, 1H), 2.97 (m, 2H), 2.38 (s, 3H), 2.27 (m, 2H), 2.10 (m, 2H), 1.84 (d, 3H), 1.74 (m, 2H).	501 [M+1]
I- 346		(3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona	0.19		(300 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.42 (m, 3H), 7.30 (m, 2H), 7.09 (m, 2H), 7.00 (m, 1H), 5.95 (q, 1H), 4.87 (s, 2H), 3.83 (m, 2H), 3.47 (m, 2H), 2.51 (m, 2H), 2.33 (m, 5H), 1.84 (d, 3H).	487 [M+1]
I- 347		3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (3- pirrolidin- 1- il)- benzamida	0.21		(300 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.91 (m, 2H), 7.65 (d, 1H), 7.42 (m, 2H), 7.00 (m, 3H) 5.99 (q, 1H), 4.85 (s, 2H), 3.60 (m, 2H), 2.76 (m, 2H), 2.63 (m, 4H), 1.84 (d, 3H), 1.77 (m, 6H).	515 [M+1]
I- 348		3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida	0.2		(300 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.86 (s, 1H), 7.70 (d, 1H), 7.50 (m, 2H), 7.00 (m, 4H), 5.99 (q, 1H), 4.86 (s, 2H), 3.60 (m, 2H), 2.78 (m, 2H), 2.63 (m, 4H), 1.85 (m, 7H).	501 [M+1]
I- 349		(3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 3- amino- pirrolidin- 1- il)- metanona	0.13		(300 MHz, $CDCl_3$) δ 7.70 (m, 5H), 7.42 (s, 1H), 7.28 (m, 1H), 7.20 (m, 1H), 6.27 (m, 1H), 4.85 (s, 2H), 3.75 (m, 5H), 3.31 (m, 2H), 2.66 (m, 1H), 2.44 (m, 1H), 1.93 (m, 3H).	473
I- 350		3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida	0.39		(300 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.84 (s, 1H), 7.65 (d, 1H), 7.46 (m, 2H), 7.05 (m, 3H), 6.83 (bs, 1H), 5.97 (q, 1H), 4.91 (s, 2H), 3.74 (m, 4H), 3.58 (m, 2H), 2.63 (m, 2H), 2.52 (m, 4H), 1.84 (m, 3H).	517 [M+1]

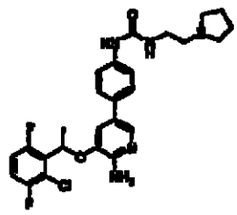
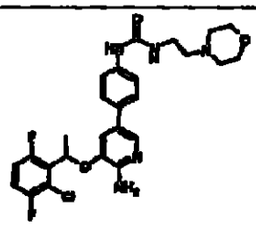
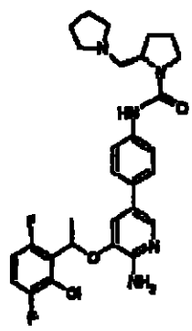
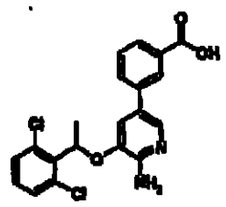
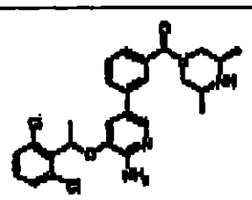
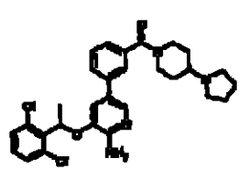
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 351		(3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.23		(300 MHz, $CDCl_3$) δ 7.88 (s. 1H), 7.45 (m, 4H), 7.05 (m, 3H), 5.98 (q, 1H), 4.86 (s, 2H), 4.45 (m, 1H), 3.64 (m, 1H), 3.44 (m, 1H), 2.64 (m, 4H), 1.83 (d, 3H), 1.70- 2.18 (m, 10H)	541 [M+1]
I- 352		(3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.15		(300 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.45 (m, 4H), 7.09 (m, 3H), 5.98 (q, 1H), 4.86 (s, 2H), 4.45 (m, 1H), 3.45 (m, 2H), 2.75 (m, 4H), 1.84 (d, 3H), 1.70- 2.18 (m, 10H)	541 [M+1]
I- 353		3- [1- (2- cloro- 3,6- difluoro- fenil)etoxi]- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina	0.23			
I- 354		3- [1- (2- cloro- 3,6- difluoro- fenil)etoxi]- 5- [3- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina	0.22			
I- 355		3- [1- (2,6- dicloro- 3- fluoro- fenil)etoxi]- 5- [4- (2- pirrolidin- 1- il- etoxi)- fenil]- piridin- 2- ilamina	0.068		(400 MHz, DMSO- d_6): d 7.74 (d, J = 2.0 Hz, 1H), 7.53 (m, 1H), 7.44 (m, 2H), 7.32 (d, J = 9.0 Hz, 2H), 7.00 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 1.6 Hz, 1H), 6.11 (m, 1H), 5.79 (s, 2H). 4.30 (m, 2H), 3.5 (m, 6H), 1.90 (m, 4H), 1.807 (d, J = 6.7 Hz, 3H).	491 [M+1]
I- 356		3- [1- (2,6- dicloro- 3- fluoro- fenil)etoxi]- 5- [4- [2- (1- metil- pirrolidin- 2- il)- etoxi]- fenil}- piridin- 2- ilamina	0.079		(400 MHz, DMSO- d_6): d 7.73 (s, 1H), 7.54 (m, 1H), 7.44 (m, 2H), 7.284 (d, J = 8.2 Hz, 2H). 6.95 (d, J = 8.6 Hz, 2H), 6.88 (s, 1H, piridina- H), 6,10 (m, 1H), 5.78 (s, 2H), 4.7 (m, 1H), 3.3 (m, 2H), 3.1 (m, 2H), 2.77 (s, 3H), 2.3 (m, 6H), 1.81 (d, J = 6.2 Hz, 3H.	504 [M+1]

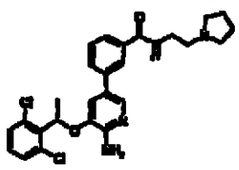
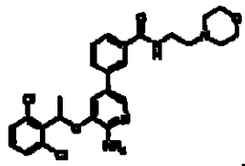
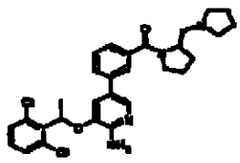
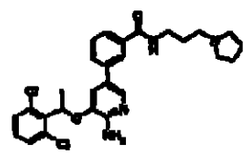
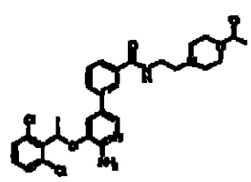
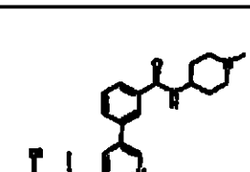
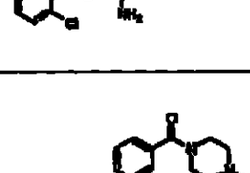
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 357		3- [1- (2,6- dicloro- 3- fluoro- fenil)etoxi]- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina	0.13		(400 MHz, DMSO- d_6): 7.72 (d, 1H), 7.53 (m, 1H), 7.44 (m, 1H), 7.33 (m, 2H), 7.03 (m, 3H), 6.23 (q, 1H), 4.35 (m, 2H) 3.95 (m, 1H), 3.0- 3.8 (m, 9H), 1.851 (d, 3H).	506 [M+1]
I- 358		3- [1- (2,6- dicloro- 3- fluoro- fenil)etoxi]- 5- [3- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina	0.22		(400 MHz, DMSO- d_6): d 7.82 (d, 1H), 7.53 (q, 1H), 7.46 (t, 1H), 7.33 (t, 1H), 7.03 (m, 3H), 6.95 (dd, 1H), 6.24 (q, 1H), 4.38 (m, 2H), 3.95 (m, 2H), 3.75 (m, 2H), 3.61 (m, 2H), 3.5 (m, 2H), 3.25(m, 2H). 1.851 (d, 3H).	506 [M+1]
I- 359		I- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenoxi)- 3- morfolin- 4- il- propan- 2- ol	0.045		(400 MHz, DMSO- d_6): d 7.73 (d, J = 1.6 Hz, 1H), 7.56 (m, 1H), 7.44 (t, J = 8.6 Hz, 1H), 7.28 (d, J = 6.7 Hz, 2H), 6.94 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 2.0 Hz, 1H), 6.11 (m, 1H), 5.75 (s, 2H), 4.88 (d, J = 2.0 Hz, 1H), 3.96 (m, 3H), 3.57 (t, J = 4.3 Hz, 4H), 2.42 (m, 6H), 1.81 (d, J = 6.7 Hz, 3H).	536 [M+1]
I- 360		3- [1- (2,6- dicloro- 3- fluoro- fenil)etoxi]- 5- [4- (2- dietilamino- etoxi)- fenil]- piridin- 2- ilamina	0.033		(400 MHz, DMSO- d_6): d 7.73 (d, J = 1.6 Hz, 1H), 7.56 (m, 1H), 7.44 (t, J = 8.6 Hz, 1H), 7.28 (d, J = 8.6 Hz, 2H), 6.92 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 1.6 Hz, 1H), 8.11 (m, 1H), 5.75 (s, 2H), 4.02 (t, J = 6.2 Hz, 2H), 2.756 (m, 2H), 2.55 (m, 4H), 1.81 (d, J = 6.7 Hz, 3H), 0.99 (t, J = 7.0 Hz, 6H).	494 [M+1]
I- 361		3- [1- (2,6- dicloro- 3- fluoro- fenil)etoxi]- 5- [4- (1- metil- piperidin- 3- ilmetoxi)- fenil]- piridin- 2- ilamina	0.043		(400 MHz, DMSO- d_6): d 7.73 (d, J = 2.0 Hz, 1H), 7.53 (m, 1H), 7.44 (t, J = 8.6 Hz, 1H), 7.27 (d, J = 8.6 Hz, 2H), 6.92 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 1.6 Hz, 1H), 8.10 (m, 1H), 5.75 (s, 2H), 3.831 (m, 2H), 2.81 (m, 1H), 2.62 (s, 1H) .2153 (s, 3H) 1.95 (m, 3H), 1.81 (d, J = 6.7 Hz, 3H), 1.72 (m, 4H).	504 [M+1]
I- 362		3- [1- (2,6- dicloro- 3- fluoro- fenil)etoxi]- 5- [4- (2- diisopropilamino- etoxi)- fenil]- piridin- 2- ilamina	0.052		(400 MHz, DMSO- d_6): d 7.73 (d, J = 2.0 Hz, 1H), 7.53 (m, 1H), 7.44 (t, J = 8.6 Hz, 1H), 7.27 (m, 2H), 6.91 (m, 2H), 6.88 (d, J = 2.0 Hz, 1H), 6.11 (m, 1H), 5.74 (s, 2H), 3.88 (t, J = 6.7 Hz, 2H), 3.02 (m, 2H), 2.76 (t, J = 6.7 Hz, 2H), 1.81 (d, J = 6.7 Hz, 3H), 0.986 (m, 12H).	520 [M+1]

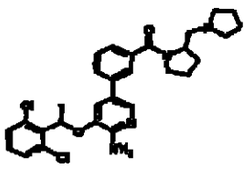
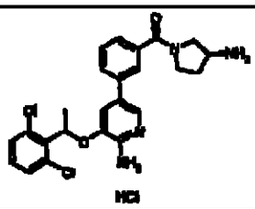
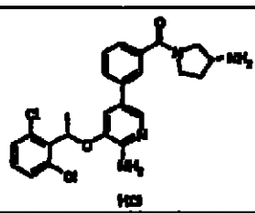
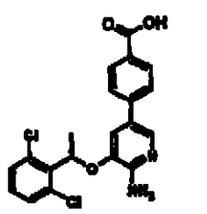
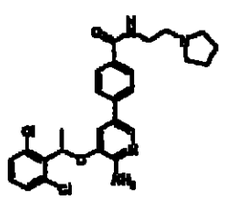
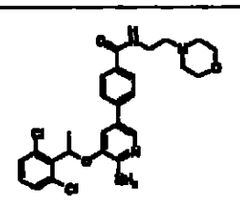
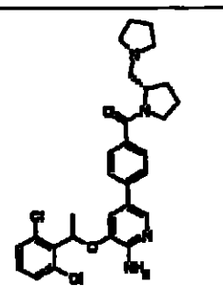
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 363		3- [1- (2,6- dicloro- 3- fluoro- fenil)etoxi]- 5- [4- (1- metil- piperidin- 4- iloxi)- fenil]- piridin- 2- ilamina	0.052		(400 MHz, DMSO- d_6): d 7.66 (d, J = 1.6 Hz, 1H), 7.49 (m, 1H), 7.377 (t, J = 8.2 Hz, 1H), 7.20 (m, 2H), 6.87 (m, 2H), 6.81 (d, J = 1.6 Hz, 1H), 6.04 (m, 1H), 5.68 (s, 2H), 4.30 (m, 1H), 2.55 (m, 2H), 2,12 (m, 5H), 1.84 (m, 2H), 1.74 (d, J = 6.7 Hz, 3H), 1,.7 (m, 2H).	490 [M+1]
I- 364		N- (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il)- fenil)- metanosulfonamida	0.1			454 [M+1]
I- 365		3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- [4- (1,1- dioxo- 1lambda*6*- isotiazolidin- 2- il)- fenil]- piridin- 2- ilamina	0.14			478 [M+1]
I- 366		N- (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il)- fenil)- metanosulfonamida	0.076		(300 MHz, $CDCl_3$) δ 9.75 (s, 1H), 7.88 (d, 1H), 7.55 (q, 1H), 7.45 (t, 1H), 7.35 (d, 2H), 7.18 (d, 2H), 6.9 (d, 1H), 6.10 (q, 1H), 5.85 (s, 2H), 2.99 (s, 3H), 1.80 (d, 3H).	470 [M+1]
I- 367		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- fenil- piridin- 2- ilamina	0.5		(300 MHz, $CDCl_3$) δ 7.80 (d, 1H), 7.55 (q, 1H), 7.45 (t, 1H), 7.35 (dd, 4H), 7.25 (m, 1H), 6.95 (d, 1H), 6.12 (q, 1H), 5.85 (s, 2H), 1.80 (d, 3H).	377 [M+1]
I- 368	 TFA	N- (4- {6- amino- 5- [(R)- 1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il)- fenil)- metanosulfonamida	0.066		(300 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.70 (d, 1H), 7.43 (m, 3H), 7.30 (ddd, 1H), 7.25 (d, 1H), 7.18 (m, 2H), 6.10 (q, 1H), 2.95 (s, 3H), 1.75 (d, 3H).	454 [M+1]
I- 369		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- tiofen- 3- il- piridin- 2- ilamina	0.055			383 [M+1]

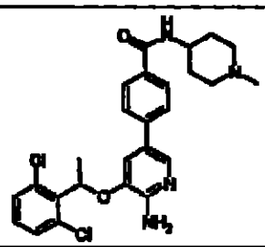
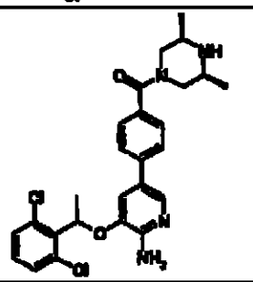
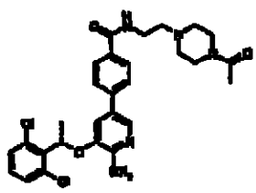
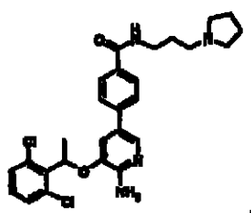
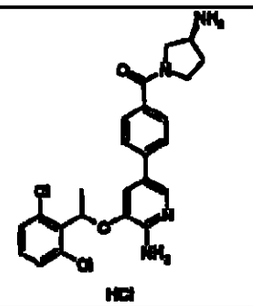
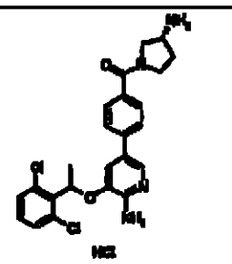
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 370		5- benzo[b]tiofen- 2- il- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina	1.95			433 [M+1]
I- 371		ácido 4- metil- piperazina- 1- carboxílico (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0.057		(300 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.40 (d, 2H), 7.32- 7.23 (m, 3H), 7.06 (t, 1H), 6.99 (s, 1H), 6.77 (ba, 1H), 6.11 (q, 1H), 5.62 (s, 2H), 3.60 (m, 4H), 2.57 (m, 4H), 2.40 (s, 3H), 1.87 (d, 3H).	518 [M+1]
I- 372		1- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (2- pirrolidin- 1- il- etil)- urea	0.21			532 [M+1]
I- 373		1- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (2- hidroxi- etil)- urea	0.064		(300 MHz, $CDCl_3$) δ 7.68 (s, 2H) 7.45 (m, 2H), 7.36 (d, 2H), 7.25 (m, 2H), 6.95 (s, 2H), 6.55 (q, 1H), 4.86 (s, 2H), 3.63 (t, 2H), 3.31 (m, 3H), 1.87 (d, 3H).	479 [M+1]
I- 374		1- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (2- hidroxi- etil)- urea	0.062		(300 MHz, $CDCl_3$) δ 7.88 (s, 1 H), 7.55 (m, 3H), 7.35 (d, 2H), 7.23 (m, 3H), 6.95 (s, 1H), 6.55 (q, 1H), 4.86 (s, 2H), 3.71 (t, 2H), 3.31 (m, 6H), 2.51 (m, 4H) 1.86 (d, 3H).	548.2 [M+1]
I- 375		ácido (R)- 3- amino- pirrolidina- 1- carboxílico (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0.053		(300 MHz, $CDCl_3$) δ 7.65 (m, 4H), 7.31 (m, 3H), 7.19 (m, 2H), 6.37 (m, 1H), 4.87 (s, 2H), 3.95 (m, 1H), 3.80 (m, 1H), 3.60 (m, 2H), 3.31 (m, 2H), 2.45 (m, 1H), 2.18 (m, 1H). 1.95 (d, 3H).	503.8 [M+1]
I- 376		ácido (S)- 3- amino- pirrolidina- 1- carboxílico (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0.052		(300 MHz, $CDCl_3$) δ 7.65 (m, 4H), 7.31 (m, 3H), 7.19 (m, 2H), 6.37 (m, 1H), 4.87 (s, 2H), 3.95 (m, 1H), 3.80 (m, 1H), 3.60 (m, 2H), 3.31 (m, 2H), 2.45 (m, 1H), 2.18 (m, 1H), 1.95 (d, 3H).	504.1 [M+1]

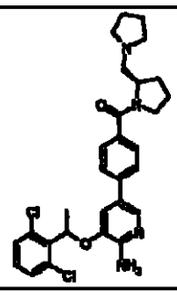
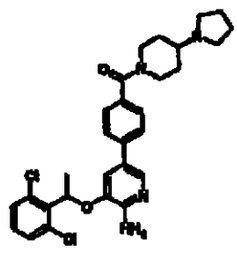
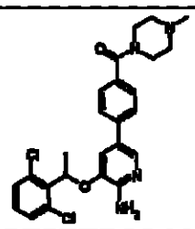
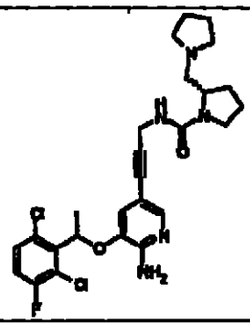
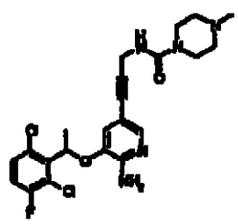
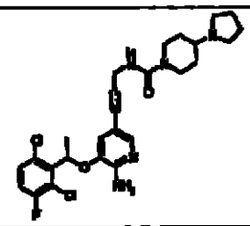
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 377		1- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (1- metil- piperidin- 4- il)- urea	0.04			534 [M+1]
I- 378		1- (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (1- metil- piperidin- 4- il)- urea	0.038			518 [M+1]
I- 379		ácido (R)- 3- amino- pirrolidina- 1- carboxílico (4- {6- amino- 5- [1- (3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0.069			488 [M+1]
I- 380		ácido (S)- 3- amino- pirrolidina- 1- carboxílico (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0.075			488 [M+1]
I- 381		1- (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (2- hidroxi- etil)- urea	0.11		(300 MHz, $CDCl_3$) δ 7.69 (d, 2H), 7.37 (d, 2H), 7.25 (d, 2H), 7.15 (m, 2H), 7.09 (d, 2H), 6.00 (q, 1H), 4.86 (s, 2H), 3.63 (t, 2H), 3.32 (m, 3H), 1.83 (d, 3H).	463 [M+1]
I- 382		ácido 4- metil- piperazino- 1- carboxílico (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il)- fenil)- amida	0.082		(300 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.41 (d, 2H), 7.29 (d, 2H), 7.09 (s, 1H), 7.05 (m, 1H), 6.95 (m, 1H), 6.56 (bs, 1H), 6.00 (q, 1H), 5.25 (s, 2H), 3.58 (m, 4H), 2.53 (m, 4H), 2.38 (s, 3H), 1.84 (d, 3H).	502 [M+1]

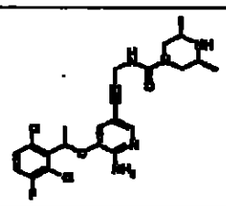
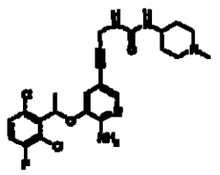
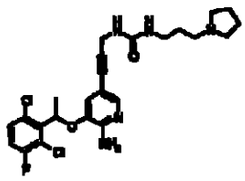
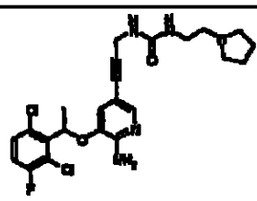
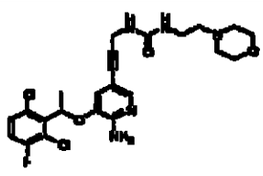
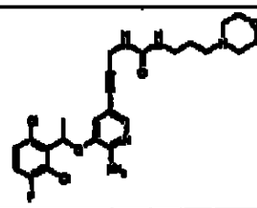
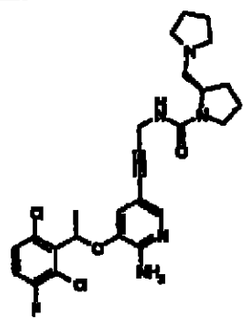
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 383		1- (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (2- pirrolidin- 1- il- etil)- urea	0.11			516 [M+1]
I- 384		1- (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (2- morfolin- 4- il- etil)- urea	0.13		(300 MHz, $CDCl_3$) δ 7.83 (d, 1H), 7.29 (m, 5H), 7.00 (m, 4H), 5.94 (q, 1H), 4.87 (ba, 2H), 3.67 (m, 4H), 3.38 (m, 2H), 2.52 (m, 4H), 1.86 (d,3H).	533.7 [M+1]
I- 385		ácido (R)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxílico (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida	0.13		(300 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.67 (d, 2H), 7.27 (d, 2H), 6.95 (m, 4H), 6.70 (q, 1H), 4.84 (s, 2H), 3.85 (m, 1H), 3.75 (m, 1H), 3.40 (m, 1H), 2.90 (m, 4H), 2.65 (m, 4H), 2.10 (m, 3H), 1.85 (d, 3H), 1.9- 1.7 (m, 3H).	535.8 [M+1]
I- 386		ácido (3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- benzoico				403 [M+1]
I- 387		(3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R,5S)- 3,5- dimetil- piperazin- 1- il)- metanona	0.16		(300 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.39 (m, 4H), 7.31 (d, 2H), 7.15 (t, 1H), 7.02 (s, 1H), 6.15 (m, 1H), 4.93 (s, 2H), 4.65 (m, 1H), 3.56 (m, 1H), 2.95 (m, 1H), 2.79 (m, 1H), 2.71 (m, 1H), 2.44 (m, 1H), 1.84 (d, 3H), 1.95 (m, 1H), 1.25 (d, 3H), 1.17 (d, 3H).	501 [M+1]
I- 388		(3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	0.1		(300 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.39 (m, 4H), 7.32 (d, 2H), 7.15 (t, 1H), 7.02 (s, 1H), 6.15 (m, 1H), 4.90 (s, 2H), 4.65 (m, 1H), 3.65 (m, 1H), 3.05 (m, 2H), 2.80 (m, 1H), 2.65 (m, 4H), 2.30 (m, 1H), 2.05 (m, 1H), 1.86 (d, 3H), 1.81 (m, 3H), 1.52 (m, 4H).	539 [M+1]

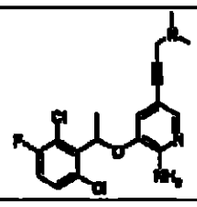
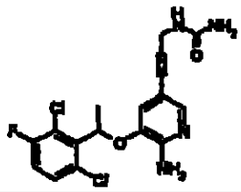
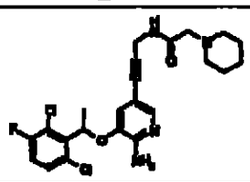
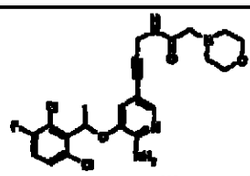
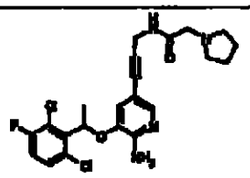
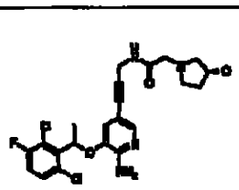
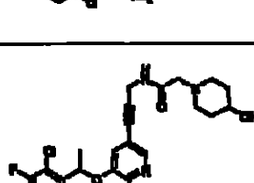
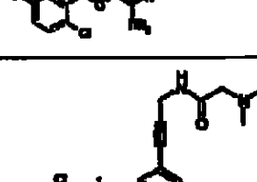
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 389		(3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida	0.13		(300 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.82 (s, 1H), 7.69 (d, 1H), 7.45 (m, 3H), 7.32 (d, 2H), 7.15 (t, 1H), 7.06 (s, 1H), 6.99 (bm, 1H), 6,16 (q, 1H), 4.93 (s, 2H), 3.61 (m, 2H), 2.78 (m, 2H) 2.63 (m, 4H), 1.87 (d, 3H), 1.82 (m, 4H).	501 [M+1]
I- 390		(3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida	0.12		(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.82 (s, 1H), 7.65 (d, 1H), 7.48 (m, 3H), 7.32 (d, 2H), 7.15 (t, 1H), 7.06 (s, 1H), 6.78 (bm, 1H), 6.16 (q, 1H), 4.95 (s, 2H), 3.73 (m, 4H), 3.59 (m, 2H), 2.62 (m, 2H), 2.51 (m, 4H), 1.87 (d, 3H).	517 [M+1]
I- 391		(3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.098		(300 MHz, $CDCl_3$) δ 7.86 (d, 1H), 7.37 (m, 4H), 7.30 (d, 2H), 7.15 (t, 1H), 7.02 (s, 1H), 6.15 (m, 1H), 4.91 (s, 2H), 4.45 (m, 1H), 3.41 (m, 2H), 2.70 (m, 4H), 1.84 (d, 3H), 1.70- 2.0 (m, 10H)	541 [M+1]
I- 392		(3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (3- pirrolidin- 1- il- propil)- benzamida	0.072		(300 MHz, $CDCl_3$) δ 8.60 (bm, 1H), 7.89 (s, 1 H), 7.65 (d, 1H), 7.45 (m, 3H), 7.32 (d, 2H), 7.15 (t, 1H), 7.04 (s, 1H), 6.17 (q, 1H), 4.89 (s, 2H), 3.62 (m, 2H), 2.78 (m, 2H), 2.66 (m, 4H), 1,86 (d, 3H), 1.83 (m, 2H), 1.79 (m, 4H).	513 [M+1]
I- 393		N- [2- (4- acetil- piperazin- 1- il)- etil]- 3- {6- amino- 5- [1- (2,6- dicloro- fenil- etoxi]- pirridin- 3- il}- benzamida	0.079		(300 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.81 (s, 1H), 7.63 (d, 1H), 7.48 (m, 3H), 7.32 (d, 2H), 7.15 (t, 1H), 7.06 (s, 1H), 6.69 (bm, 1H), 6.16 (q, 1H), 4.94 (s, 2H), 3.65 (m, 4H), 3.50 (m, 2H), 2.62 (m, 2H), 2.52 (m, 4H), 2.09 (s, 3H), 1.87 (d, 3H),	556 [M+1]
I- 394		(3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (1- metil- piperidin- 4- il)- benzamida	0.061		(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.73 (s, 1 H), 7.65 (d, 1H) 7.50(d, 1H), 7.43 (t, 1H), 7.32 (d, 2H), 7.16 (t ,1H), 7.04 (s, 1H), 6.15 (m, 1H), 6.05 (bd, 1H), 4.92 (s, 2H), 4.03 (m, 1H), 2.94 (m, 2H), 2.38 (s, 3H), 2.26 (m, 2H), 2.09 (m, 2H), 1.86 (d, 3H), 1.70 (m, 2H).	499 [M+1]
I- 395		(3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- pirenazin- 1- il)- metanona	0.058		(300 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.40 (m, 4H), 7.30 (d, 2H), 7.16 (t, 1H), 7.02 (s, 1H), 6.15 (m, 1H), 4.93 (s, 2H), 3.82 (m, 2H), 3.45 (m, 2H), 2.52 (m, 2H), 2.38 (m, 2H), 2.33 (s, 3H), 1.86 (d, 2H).	487 [M+1]

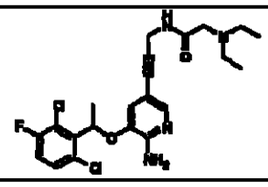
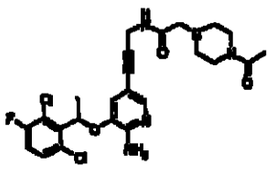
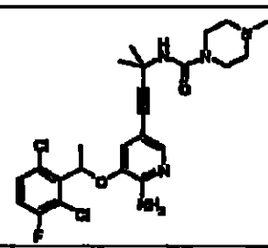
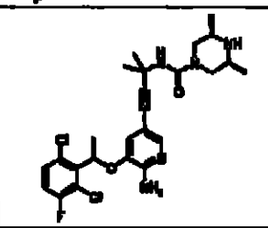
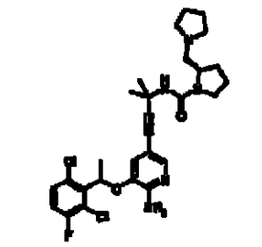
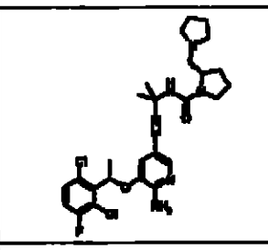
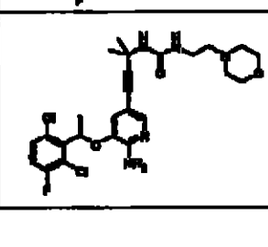
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 396		(3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.18		(300 MHz, $CDCl_3$) δ 7.86 (d, 1H), 7.37 (m, 4H), 7.30 (d, 2H), 7.15 (t, 1H), 7.02 (s, 1H), 6,15 (m, 1H), 4.91 (s, 2H), 4.45 (m, 1H), 3.41 (m, 2H), 2.70 (m, 4H), 1.84 (d, 3H), 1.70- 2.0 (m, 10H)	541 [M+1]
I- 397	 HCl	(3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil- ((S)- 3- amino- pirrolidin- 1- il)- metanona	0.055		(300 MHz, CD_3OD) δ 7.74 (s, 1H), 7.69- 7.43 (m, 6H), 7.32 (t, 1H), 7.22 (s, 1H). 6.42 (m, 1H), 4.05- 3.60 (m, 4H), 3.50 (m, 1H), 2.50 (m, 1H), 2.18 (m, 1H), 1.90 (d, 3H).	471 [M+1]
I- 398	 HCl	(3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil- ((R)- 3- amino- pirrolidin- 1- il)- metanona	0.072		(300 MHz, CD_3OD) δ 7.74 (s, 1H), 7.69- 7.43 (m, 6H), 7.32 (t, 1H), 7.22 (s, 1H), 6.42 (m, 1H), 4.05- 3.60 (m, 4H), 3.50 (m, 1H), 2.50 (m, 1H), 2.18 (m, 1H), 1.90 (d, 3H).	471 [M+1]
I- 399		ácido 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- benzoico				403 [M+1]
I- 400		4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida	0.059		(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.79 (d, 2H), 7.43 (d, 2H), 7.32 (d, 2H), 7.15 (t, 1H), 7.02 (s, 1H). 6.87 (bm, 1H), 6.15 (q, 1H), 4.93 (s, 2H), 3.56 (m, 2H), 2.72 (m, 2H), 2.58 (m, 4H), 1.87 (d, 3H), 1.80 (m, 4H).	501 [M+1]
I- 401		4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida	0.073		(300 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.79 (d, 2H), 7.44 (d, 2H), 7.32 (d, 2H). 7.15 (t, 1H), 7.03 (s, 1H), 6.77 (bm, 1H), 6.15 (q, 1H), 4.95 (s, 2H), 3.74 (m, 4H), 3.57 (m, 2H). 2.61 (m, 2H), 2.52 (m, 4H), 1.87 (d, 3H).	515 [M+1]
I- 402		(4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.068		(300 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.52 (m, 2H), 7.39 (d, 2H), 7.31 (d, 2H) 7.15 (t, 1H), 7.01 (s, 1H), 6.15 (q, 1H), 4.91 (s, 2H), 4.45 (m, 1H), 3.41 (m, 2H), 2.70 (m, 4H), 1.86 (d, 3H), 1.70- 2.0 (m, 10H)	539 [M+1]

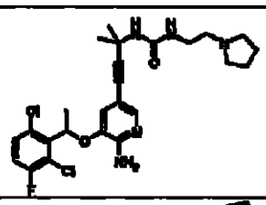
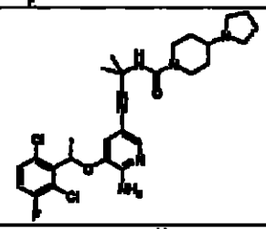
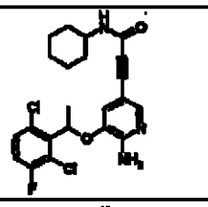
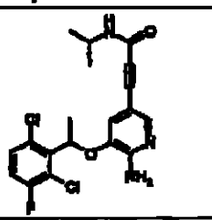
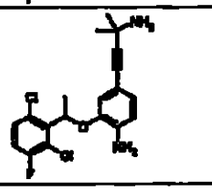
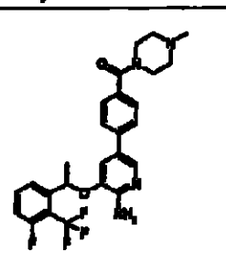
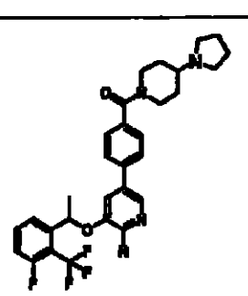
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 403		(4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil- N- (1- metil- piperidin- 4- il)- benzamida	0.062		(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.76 (d, 2H), 7.42 (d, 2H), 7.31 (d, 2H), 7.15 (t, 1H), 7.02 (s, 1H), 6.15 (q, 1H), 5.97 (bd, 1H), 4.94 (s, 2H), 4.03 (m, 1H), 2.85 (m, 2H), 2.32 (s, 3H), 2.18 (m, 2H), 2.06 (m, 2H), 1.86 (d, 3H), 1.60 (m, 2H),	501 [M+1]
I- 404		(4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R,5S)- 3,5- dimetil- piperazin- 1- il)- metanona	0.052		(300 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.41 (m, 4H), 7.32 (d, 2H), 7.15 (t, 1H), 7.02 (s, 1H), 6.15 (q, 1H), 4.92 (s, 2H), 4.62 (m, 1H), 3.66 (m, 1H), 2.82 (m, 2H), 2.68 (m, 1H), 2.40 (m, 1H), 1.87 (d, 3H), 1.65 (m, 1H), 1.15 (d, 3H), 0.98 (d, 3H).	499 [M+1]
I- 405		N- [2- (4- acetil- piperazin- 1- il)- etil]- 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- benzamida	0.062		(300 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.78 (d, 2H), 7.44 (d, 2H), 7.32 (d, 2H), 7.15 (t, 1H), 7.03 (s, 1H), 6.69 (bm, 1H), 6.15 (q, 1H), 4.96 (s, 2H), 3.66 (m, 2H), 3.61 (m, 2H), 3.50 (m, 2H), 2.62 (m, 2H), 2.52 (m, 4H), 2.10 (s, 3H), 1.87 (d, 3H).	556 [M+1]
I- 406		(4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- N- (3- pirrolidin- 1- il- propil)- benzamida	0.061		(300 MHz, $CDCl_3$) δ 8.80 (bm, 1H), 7.90 (s, 1H), 7,79 (d, 2H), 7.40 (d, 2H), 7.31 (d, 2H), 7.15 (t, 1H), 7.02 (s, 1H), 6.15 (q, 1H), 4.91 (s, 2H), 3.62 (m, 2H), 2.78 (m, 2H), 2,66 (m, 4H), 1.87 (d, 3H), 1.85 (m, 4H), 1.25 (m, 2H).	513 [M+1]
I- 407	 HCl	(4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 3- aminopirrolidin- 1- il)- metanona	0.05		(300 MHz, CD_3OD) δ 7.74- 7.24 (m, 9H), 6.39 (m, 1H), 4.05- 3.60 (m, 4H), 3.50 (m, 1H), 2.50 (m, 1H), 2.18 (m, 1H), 1.90 (d, 3H)	471 [M+1]
I- 408	 HCl	(4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona	0.049		(300MHZ, CD_3OD) δ 7.74- 7.24 (m, 9H), 6.39 (m, 1H), 4.05- 3.60 (m, 4H), 3.50 (m, 1H), 2.50 (m, 1H), 2.18 (m, 1H), 1.90 (d, 3H).	471 [M+1]

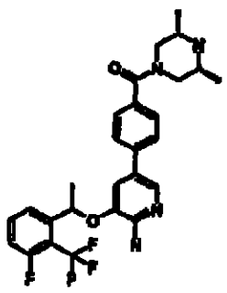
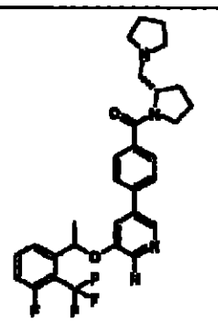
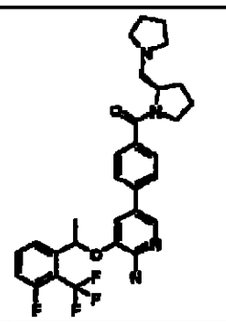
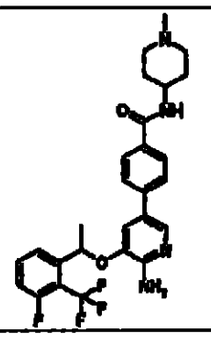
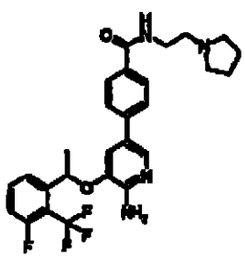
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 409		(4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.081		(300 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.52 (m, 2H), 7.39 (d, 2H), 7.31 (d, 2H), 7.15 (t, 1H), 7.01 (s, 1H), 6.15 (q, 1H), 4.91 (s, 2H), 4.45 (m, 1H), 3.41(m, 2H), 2.70 (m, 4H), 1.86 (d, 3H), 1.70- 2.0 (m, 10H)	539 [M+1]
I- 410		(4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	0.055		(300 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.39 (m, 4H), 7.32 (d, 2H), 7.17 (t, 1H), 7.01 (s, 1H), 6.15 (q, 1H), 4.91 (s, 2H), 4.60 (m, 1H), 3.76 (m, 1H), 3.00 (m, 2H), 2.60 (m, 4H), 2.28 (m, 1H), 1.95 (m, 2H), 1.86 (d, 3H), 1.81 (m, 4H), 1.56 (m, 2H).	541 [M+1]
I- 411		(4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona	0.053		(300 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.40 (m, 4H), 7.31 (d, 2H), 7.15 (t, 1H), 7.01 (s, 1H), 6.15 (q, 1H), 4.92 (s, 2H), 3.78 (m, 2H), 3.52 (m, 2H), 2.41 (m, 4H), 2.34 (s, 3H), 1.86 (d, 3H).	487 [M+1]
I- 412		ácido (S)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxílico (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- amida	0.067		(300 MHz, $CDCl_3$) δ 9.05 (br, 1H), 7.70 (s, 1H), 7.05 (t, 1H), 6.70 (s, 1H), 6.02 (q, 1H), 5.01 (s, 2H), 4.15 (dd, 2H), 3.75 (m, 2H), 3.25 (m, 1H), 2.75 (m, 3H), 2.45 (m, 3H), 2.05 (m, 1H), 1.78 (d, 3H), 1.65 (br, 7H).	534 [M+1]
I- 413		ácido 4- metil- piperazina- 1- carboxílico (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- amida	0.056		(300 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.30 (m, 2H), 7.05 (t, 1H), 6.75 (s, 1H), 6.02 (q, 1H), 5.01 (s, 2H), 4.20 (d, 2H), 3.45 (m, 4H), 2.45 (m, 4H), 2.25(s, 3H), 1.81 (d, 3H).	480 [M+1]
I- 414		ácido 4- pirrolidin- 1- il- piperidina- 1- carboxílico (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- amida	0.058		(300 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.30 (m, 2H), 7.10 (t, 1H), 6.70 (s, 1H), 6.02 (q, 1H), 5.01 (s, 2H), 4.20 (d, 2H), 3.89 (d, 1H), 2.89 (t, 2H), 2,55 (s, 4H), 2.21 (m, 2H), 1.90 (d, 2H), 1.81 (d, 3H), 1.45 (m, 2H), 1.25 (m, 2H).	534 [M+1]

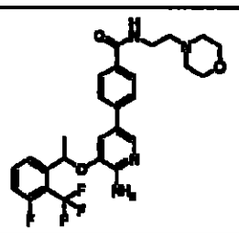
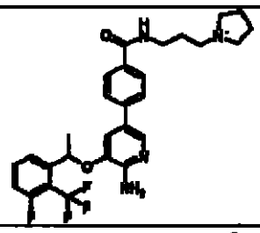
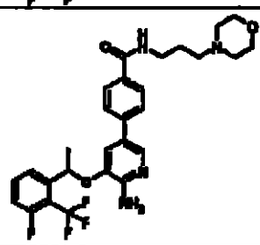
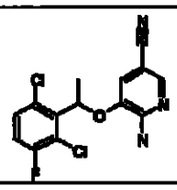
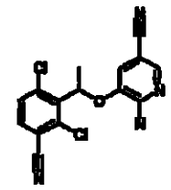
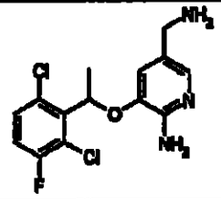
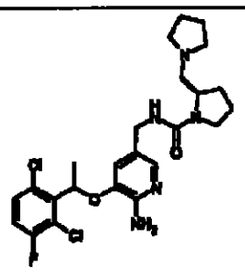
No.	Estructura	Nombre	Met IC$_{50}$ (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I-415		ácido (3R, 5S)- 3,5- dimetil- piperazina- 1- carboxílico (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- amida	0.063		(300 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.30 (m, 2H), 7.05 (t, 1H), 6.75 (s, 1H), 6.02 (q, 1H), 5.01 (s, 2H), 4.78 (s, 1H), 4.20 (d, 2H), 3.85 (d, 1H), 2.85 (m, 4H), 2.45 (t, 1H), 1.89 (s, 3H), 1.01 (d, 6H).	494 [M+1]
I-416		1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 3- (1- metil- piperidin- 4- il)- urea	0.051		(300 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.30 (m, 2H), 7.05 (t, 1H), 6.70 (s, 1H), 6.00 (q, 1H), 5.25 (m, 1H), 5.05 (s, 2H), 4.80 (d, 1H), 4.15 (d, 2H), 2.75 (d, 2H), 2.20 (s, 3H), 2.10 (t, 2H), 1.95 (d, 2H), 1.75 (d, 3H), 1.45 (d, 2H).	494 [M+1]
I-417		1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 3- (3- pirrolidin- 1- il- propil)- urea	0.062		(300 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.30 (m, 2H), 7.05 (t, 1H), 6.70 (s, 1H), 6.00 (q, 1H), 5.30 (m, 1H), 5.01 (s, 2H), 4.15 (d, 2H), 3.25 (m, 2H), 2.50 (m, 6H), 1.80 (d, 3H), 1.82 (m, 4H), 1.60 (m, 2H).	508 [M+1]
I-418		1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 3- (2- pirrolidin- 1- il- propil)- urea	0.052		(300 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.30 (m, 2H), 7.05 (t, 1H), 6.70 (s, 1H), 5.00 (q, 1H), 5.45 (s, 1H), 5.15 (s, 2H), 4.15 (d, 2H), 3.25 (m, 2H), 2.60 (t, 2H), 2.50 (m, 4H), 1.80 (d, 3H), 1.70 (s, 4H).	496 [M+1]
I-419		1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 3- (2- morfolin- 4- il- etil)- urea	0.055		(300 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.28 (m, 2H), 7.05 (t, 1H), 6.70 (s, 1H), 6.00 (q, 1H), 5.25 (s, 1H) 5.15 (s, 2H), 4.15 (d, 2H), 3.65 (m, 4H), 3.25 (m, 2H), 2.45 (m, 6H), 1.80 (d, 3H).	510 [M+1]
I-420		1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 3- (3- morfolin- 4- il- propil)- urea	0.064		(300 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.30 (m, 2H), 7.05 (t, 1H), 6.70 (s, 1H), 6.00 (q, 1H), 5.10 (s, 2H), 4.15 (d, 2H), 3.70 (m, 6H), 3.20 (s, 2H), 2.50 (m, 4H), 1.80 (d, 3H), 1.65 (m, 2H).	524 [M+1]
I-421		ácido (R)- 2- pirrolidina- 1- ilmetil- pirrolidina- 1- carboxílico (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- amida	0.071		(300 MHz, $CDCl_3$) δ 9.05 (br, 1H), 7.70 (s, 1H), 7.05 (t, 1H), 6.70 (s, 1H), 6.02 (q, 1H), 5.01 (s, 2H), 4.15 (dd, 2H), 3.75 (m, 2H), 3.25 (m, 1H), 2.75 (m, 3H), 2.45 (m, 3H), 2.05 (m, 1H), 1.78 (d, 3H), 1.65 (br, 7H).	534 [M+1]

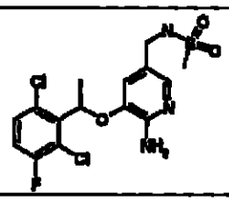
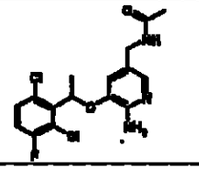
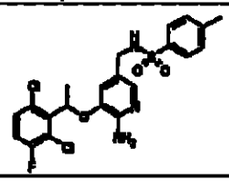
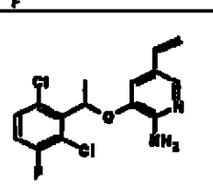
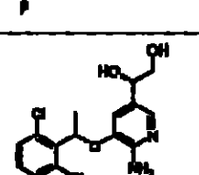
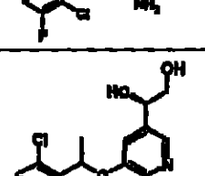
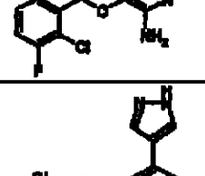
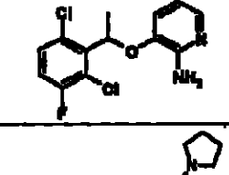
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 422		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3- dimetilamino- prop- 1- inil)- piridin- 2- ilamina	0.071			382 [M+1]
I- 423		3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- urea	0.062			397 [M+1]
I- 424		N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- piperidin- 1- il- acetamida	0.016		(300 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.45 (bm, 1H), 7.31 (dd, 1H), 7.07 (t, 1H), 6.73 (s, 1H), 6.00 (q, 1H), 4.99 (s, 2H), 4.26 (d, 2H), 2.98 (s, 2H), 2.46 (m, 4H), 1.81 (d, 3H), 1.59 (m, 4H), 1.45 (m, 2H).	579 [M+1]
I- 425		N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- morfolin- 4- il- acetamida	0.27		(300 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.45 (bm 1H), 7.31 (m, 2H), 7.08 (t, 1H), 6.71 (s, 1H), 6.00 (q, 1H), 5.02 (s, 2H), 4.27 (d, 2H), 3.73 (m. 4H), 3.05 (s, 2H), 2.54 (m, 4H), 1.81 (d, 3H).	481 [M+1]
I- 426		N- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- pirrolidin- 1- il- acetamida	<0.00091		(300 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.37 (bm, 1H), 7.31 (dd, 1H), 7.08 (t, 1H), 6.72 (s, 1H), 6.00 (q, 1H), 5.01 (s, 2H), 4.27 (d, 2H), 3.18 (s, 2H), 2.63 (m, 4H), 2.01 (m, 2H), 1.81 (d, 3H), 1.80 (m, 2H).	465 [M+1]
I- 427		N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- ((R)- 3- hidroxi- pirrolidin- 1- il- acetamida	0.011		(300 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.45 (bm, 1H), 7.31 (dd, 1H), 7.07 (t, 1H), 6.72 (s, 1H), 5.99 (q, 1H), 5.06 (s, 2H), 4.42 (m, 1H), 4.25 (m, 2H), 3.21 (s, 2H), 3.00 (m. 1H), 2.80 (m, 1H), 2.71 (m, 1H), 2.45 (m, 1H), 2.22 (m, 1H), 1.79 (d, 3H), 1.78 (m, 2H).	481 [M+1]
I- 428		N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- (4- hidroxi- piperidin- 1- il)- acetamida	0.012		(300 MHz, $CDCl_3$) δ 7.73 (d, 1H), 7.38 (bm, 1H), 7.31 (dd, 1H), 7.08 (dd, 1H), 6.72 (d, 1H), 6.00 (q, 1H), 5.03 (s, 2H), 4.26 (d, 2H), 3.74 (m, 1H), 3.02 (s, 2H), 2.78 (m, 2H); 2.32 (m, 2H), 1.92 (m, 4H), 1.80 (d, 3H),	495 [M+1]
I- 429		N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- dimetilamino- acetamida	0.022		(300 MHz, $CDCl_3$) δ 7.73 (d, 1H), 7.38 (bm, 1H), 7.31 (dd, 1H), 7.08 (dd, 1H), 6.72 (d, 1H), 6.00 (q, 1H), 4.99 (s, 2H), 4.26 (d, 2H), 2.98 (s, 2H), 2.31 (s, 6H), 1.80 (d, 3H).	439 [M+1]

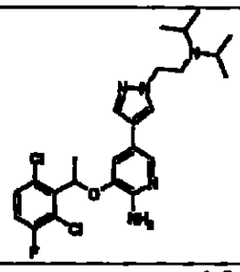
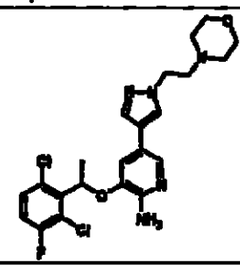
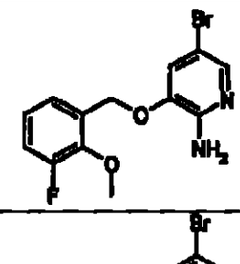
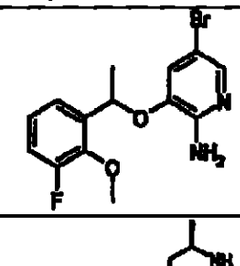
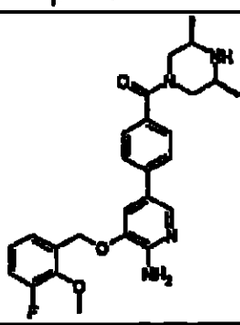
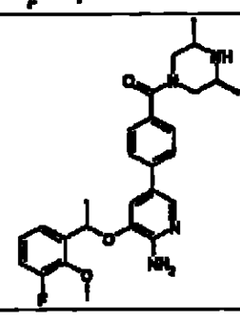
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 430		N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- dietilamino- acetamida	0.013		(300 MHz, $CDCl_3$) δ 7.73 (d, 1H), 7.59 (bm, 1H), 7.30 (dd, 1H), 7.07 (dd, 1H), 6.72 (d, 1H), 6.00 (q, 1H), 4.98 (s, 2H), 4.25 (d, 2H), 3.05 (s, 2H), 2.57 (dd, 4H), 1.80 (d, 3H), 1.03 (t, 6H)	467 [M+1]
I- 431		2- (4- acetil- piperazin- 1- il)- N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- acetamida	0.027		(300 MHz, $CDCl_3$) δ 7.73 (d, 1H), 7.31 (dd, 1H), 7.25 (bm, 1H), 7.08 (dd, 1H), 6.71 (d, 1H), 6.00 (q, 1H), 5.04 (s, 2H), 4.27 (d, 2H), 3.66 (m, 2H), 3.52 (m, 2H), 3.08 (s, 2H), 2.78 (m, 2H), 2.32 (m, 2H), 2.53 (m, 4H), 2.10 (s, 3H), 1.81 (d, 3H).	522 [M+1]
I- 432		ácido 4- metil- piperazina- 1- carboxílico (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- amida	Hi 0.61		(300 MHz, $CDCl_3$) δ 7.73 (d, 1H), 7.30 (dd, 1H), 7.07 (t, 1H), 6,78 (d, 1H), 6.01 (q, 1H), 5.01 (s, 2H), 4.64 (s, 1H), 3.38 (m, 4H), 2.42 (m, 4H), 2.31 (s, 3H), 1.79 (d, 3H), 1.70 (s, 6H).	508 [M+1]
I- 433		ácido (3R,5S)- 3,5- dimetil- piperazin- 1- carboxílico (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- amida	Hi 1.5		(300 MHz, $CDCl_3$) δ 7.74 (s, 1 H), 7.30 (dd, 1H), 7.07 (t, 1H), 6.79 (s, 1H), 6.01 (q, 1H), 4.93 (s, 2H), 4.59 (s, 1H), 3.75 (m, 2H), 2.82 (m, 2H), 2.35 (m, 2H), 1.80 (d, 3H), 1.71 (s, 6H), 1.09 (d, 6H).	522 [M+1]
I- 434		ácido (R)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxílico (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- amida	Hi 1.22		(300 MHz, $CDCl_3$) δ 8.44 (bs, 1H), 7.72 (d, 1H), 7.30 (dd, 1H), 7.07 (t, 1H), 6.79 (s, 1H), 6.01 (q, 1H), 4.87 (s, 2H), 3.75 (m, 1H), 3.25 (m, 1H), 2.68 (m, 2H), 2.56 (m, 2H), 2.40 (m, 1H), 2.05 (m, 1H), 1.82- 1.68 (m, 17H), 1.56 (m, 1H).	562 [M+1]
I- 435		ácido (S)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxílico (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- amida	Hi 1.58		(300 MHz, $CDCl_3$) δ 8.44 (bs, 1H), 7.72 (s, 1H), 7.30 (dd, 1H), 7.07 (t, 1H), 6.79 (s, 1H), 6.01 (q, 1H), 4.87 (s, 2H), 3.75 (m, 1H), 3.25 (m, 1H), 2.68 (m, 2H), 2.56 (m, 2H), 2.40 (m, 1H), 2.05 (m, 1H), 1.82- 1.68 (m, 17H), 1.56 (m, 1H).	562 [M+1]
I- 436		1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- 3- (2- morfolin- 4- il- etil)- urea	Hi 1.11		(300 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.31 (dd, 1H), 7.08 (t, 1H), 6.75 (s, 1H), 6.01 (q, 1H). 5.53 (bm, 1H), 5.00 (s, 2H), 4.66 (bs, 1H), 3.56 (m, 4H), 3.32 (m, 2H), 2.45 (m, 2H), 2.35 (m, 4H), 1.81 (d, 3H), 1.64 (s, 6H).	538 [M+1]

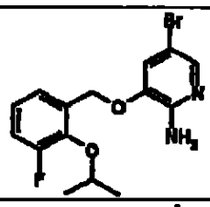
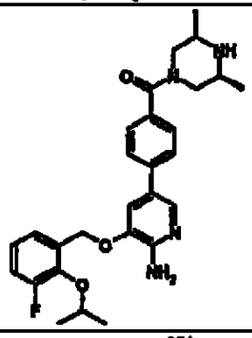
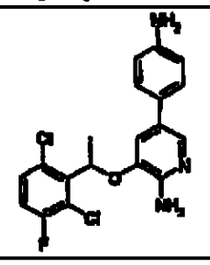
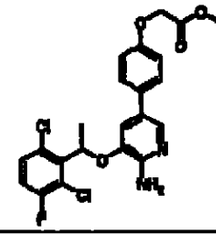
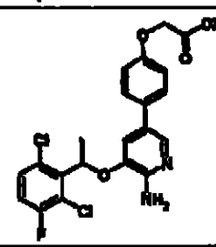
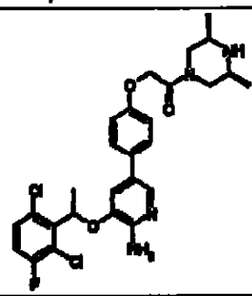
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I-437		1-(3-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-1,1-dimetil-prop-2-inil)-3-(2-pirrolidin-1-il-etil)-urea	Hi 0.61		(300 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.31 (dd, 1H), 7.08 (t, 1H), 6.77 (s, 1H), 6.01 (q, 1H), 5.68 (bm, 1H), 5.14 (bs, 1H), 5.01 (s, 2H), 3.30 (m, 2H), 2.65 (m, 2H), 2.50 (m, 4H), 1.81 (d, 3H), 1.68 (m, 4H), 1.63 (s, 6H).	522 [M+1]
I-438		ácido 4-pirrolidin-1-il-piperidina-1-carboxílico (3-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-1,1-dimetil-prop-2-inil)-amida	Hi 0.72		(300 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.31 (dd, 1H), 7.07 (t, 1H), 6.79 (s, 1H), 6.01 (q, 1H), 5.68 (bm, 1H), 4.95 (s, 2H), 4.68 (bs, 1H), 3.88 (m, 2H), 2.82 (m, 2H), 2.58 (m, 4H), 2.28 (m, 1H), 1.92 (m, 2H), 1.81 (d, 3H), 1.80 (m, 4H), 1.70 (s, 6H), 1.50 (m, 2H).	562 [M+1]
I-439		ácido ciclohexilamida (3-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-propinoico	Hi 0.46		(300 MHz, $CDCl_3$) δ 7.85 (d, 1H), 7.31 (dd, 1H), 7.09 (t, 1H), 6.78 (d, 1H), 6.00 (q, 1H), 5.69 (bd, 1H), 5.14 (s, 2H), 4.12 (m, 1H), 1.81 ds, 3H), 1.20 (d, 6H)	410 [M+1]
I-440		ácido isopropilamida (3-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-propinoico	Hi 0.43		(300 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.31 (dd, 1H), 7.09 (t, 1H), 6.79 (s, 1H), 6.00 (q, 1H), 5.72 (bd, 1H), 5.14 (s, 2H), 3.82 (m, 1H), 1.95 (m, 2H), 1.80 (d, 3H), 1.72 (m, 2H), 1.65 (m, 2H), 1.38 (m, 2H), 1.20 (m, 2H).	450 [M+1]
I-441		4-(3-amino-3-metil-but-1-inil)-2-[1-(2,6-dicloro-3-floro-fenil)-etoxi]-fenilamina	Hi 1.06		(300 MHz, CD_3OD) δ 7.60 (d, 1H), 7.45 (dd, 1H), 7.25 (t, 1H), 6.66 (d, 1H), 6.06 (q, 1H), 1.84 (d, 3H), 1.66 (s, 6H).	382 [M+1]
I-442		(4-{6-amino-5-[1-(3-fluoro-2-trifluorometil-fenil)-etoxi]-piridin-3-il}-fenil)-(4-metil-piperazin-1-il)-metanona	16% a 1uM		(300 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.51 (m, 1H), 7.40 (m, 5H), 7.10 (m, 1H), 6.90 (s, 1H), 5.80 (q, 1H), 4.94 (s, 2H), 3.58 (m, 4H), 2.53 (m, 4H), 2.32 (s, 3H), 1.84 (d, 3H).	503 [M+1]
I-443		(4-{6-amino-5-[1-(3-fluoro-2-trifluorometil-fenil)-etoxi]-piridin-3-il}-fenil)-(4-pirrolidin-1-il-piperidin-1-il)-metanona	13% a 1uM		(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.54 (m, 1H), 7.32 (d, 5H), 7.17 (m, 1H), 6.90 (d, 1H), 5.79 (q, 1H), 4.93 (s, 2H), 4.60 (m, 1H), 3.80 (m, 1H), 2.95 (m, 2H), 2.64 (m, 4H), 2.34 (m, 1H), 1.95 (m, 2H), 1.81 (m, 4H), 1.73 (d, 3H), 1.56 (m, 2H).	557 [M+1]

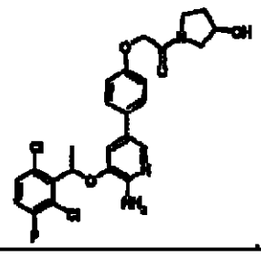
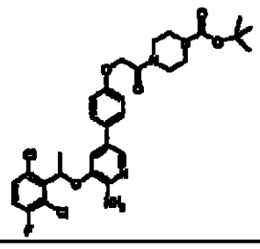
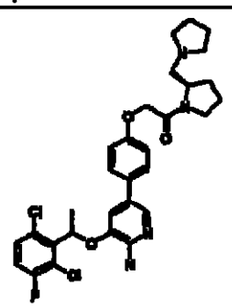
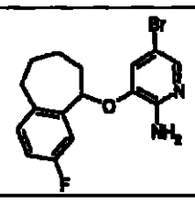
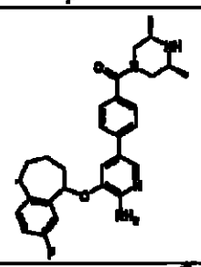
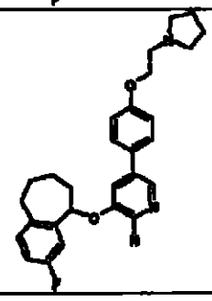
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I-444		(4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R,5S)- 3,5- dimetil- piperazin- 1- il)- metanona	10% a 1uM		(300 MHz, $CDCl_3$) δ 7.9 (d, 1H), 7.50 (m, 1H), 7.36 (m, 5H), 7.11 (m, 1H), 6.90 (s, 1H), 5.81 (q, 1H), 4.93 (s, 2H), 4.62 (m, 1H), 3.66 (m, 1H), 2.85 (m, 2H), 2.65 (m, 1H), 2.40 (m, 1H), 1.73 (d, 3H), 1.10 (m, 7H).	517 [M+1]
I-445		(4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	15% a 1uM		(300 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.73 (m, 1H), 7.53 (m, 3H), 7.34 (d, 2H), 7.13 (m, 1H), 6.90 (s, 1H), 5.80 (q, 1H), 4.93 (s, 2H). 4.45 (m, 1H), 3.50 (m, 2H), 2.70 (m. 4H), 1.73 (d, 3H), 1.20- 2.0 (m, 10H).	557 [M+1]
I-446		(4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	12% a 1uM		(300 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.73 (m, 1H), 7.53 (m, 3H), 7.34 (d, 2H), 7.13 (m, 1H), 6.90 (s, 1H), 5.80 (q, 1H), 4.93 (s, 2H), 4.45 (m, 1H), 3.50 (m, 2H), 2.70 (m. 4H), 1.73 (d, 3H), 1.20- 2.0 (m, 10H).	557 [M+1]
I-449		(4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- N- (1- metil- piperidin- 4- il)- benzamida	12% a 1uM		(300 MHz, $CDCl_3$) δ 7.90 (d, 1H), 7.75 (d, 2H), 7.72 (m, 1H), 7.52 (m, 1H), 7.48 (d, 2H), 7.10 (m, 1H), 6,89 (d, 1H), 6.00 (bd, 1H), 5.80 (q, 1H), 4.93 (s, 2H), 4.02 (m, 1H), 2.85 (m, 2H), 2.31 (s. 3H), 2.16 (m. 2H), 2.05 (m, 2H), 1.73 (d, 3H), 1.62 (m, 2H).	517 [M+1]
I-450		4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida	7% a 1uM st		(300 MHz, $CDCl_3$) δ 7.90 (d, 1H), 7.79 (d, 2H), 7.55 (m, 2H), 7.48 (d, 2H), 7.13 (m, 1H), 7.08 (ba, 1H), 6.90 (s, 1H), 5.80 (q, 1H), 4.94 (s, 2H), 3.58 (m, 2H), 2.78 (m, 2H), 2.62 (m, 4H), 1.81 (m, 4H), 1.72 (d, 3H).	517 [M+1]

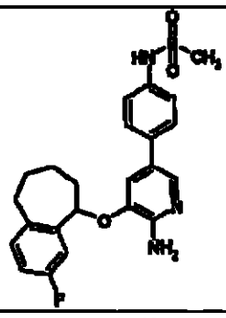
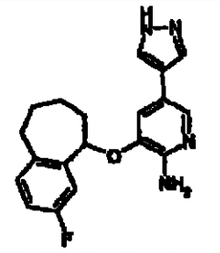
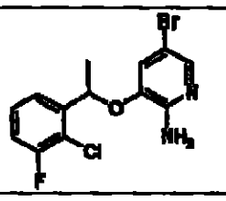
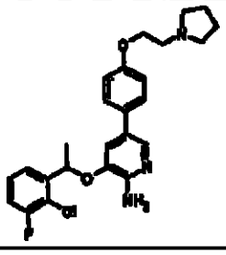
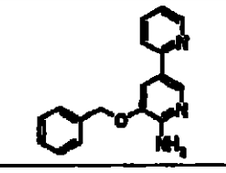
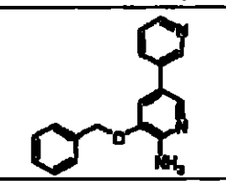
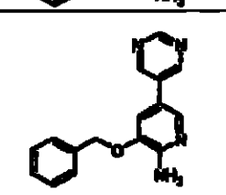
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 451		4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida	12% a 1uM		(300 MHz, $CDCl_3$) δ 7.91 (d, 1H), 7.78 (d, 2H), 7.51 (m, 2H), 7.39 (d, 2H), 7.10 (m, 1H), 6.91 (d, 1H), 6.76 (bs, 1H), 5.82 (q, 1H), 4.97 (s, 2H), 3.72 (m, 4H), 3.57 (m, 2H), 2.62 (m, 2H), 2,52 (m, 4H), 1.73 (d, 3H).	533 [M+1]
I- 452		4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- N- (3- pirrolidin- 1- il- propil)- benzamida	3% a 1uM		(300 MHz, $CDCl_3$) δ 8.81 (s, 1H), 7.92 (s, 1H), 7.78 (d, 2H), 7.53 (m, 1H), 7.48 (d, 2H), 7.13 (m, 1H), 6.90 (s, 1H), 5.80 (q, 1H), 4.90 (s, 2H), 3.60 (m, 2H), 2.78 (m, 2H), 2,66 (m, 4H), 1.85 (m, 6H), 1.73 (d, 3H).	531 [M+1]
I- 453		4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- N- (3- morfolin- 4- il- propil)- benzamida	10% a 1uM		(300 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.80 (d, 2H), 7.53 (m. 3H), 7.38 (d, 2H), 7.10 (m, 1H), 6.91 (d, 1H), 5.82 (q, 1H), 4.95 (s, 2H), 3.70 (m, 4H), 3.57 (m, 2H), 2.54 (m, 6H), 1.81 (m, 2H), 1.73 (d, 3H).	547 [M+1]
I- 454		6- amino- 5- [1- (2,6.dicloro- 3- fluoro- fenil)- etoxi]- nicotinonitrilo	7% a 1uM		(400 MHz, DMSO- d_6) δ7.93 (s, 1H), 7.56 (m, 1H), 7.46 (t, 1H), 6.88 (br, 2H), 6.76 (s, 1H), 6.02 (q, 1H), 1.77 (d, 3H).	325 [M- 1]
I- 455		6- amino- 5- [1- (2,6.dicloro- 3- ciano- fenil)- etoxi]- nicotinonitrilo	6% a 1uM		(400 MHz, DMSO- d_6) δ 8.00 (s, 1H), 7.81 (d, 1H), 7.07 (t, 2H), 5.78 (d, 1H), 1.74 (d, 3H).	332 [M- 1]
I- 456		5- aminometil- 3- [1- (2,6.dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina	0% a 1uM		(400 MHz, DMSO- d_6) δ 7.53 (m, 1H), 7.43 (m, 2H). 6.76 (s, 1H), 5.98 (q, 1H), 5.47 (br, 2H), 1.74 (d, 3H)	331 [M+1]
I- 457		ácido (R)- 2- pirrolidin- 1- ilmetil- pirrotidina- 1- carboxílico {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- ilmetil}- amida	1% a 1uM		(400 MHz, DMSO- d_6) δ 9.58 (s, 1H), 7.93 (s, 1H), 7.55 (m, 1H), 7.40 (s, 1H), 6.59 (dd, 1H), 6.80 (d, 1H), 6.06 (t, 1H), 4,19 (dd, 1H), 4.10 (dd, 1H), 3.94 (dd, 1H), 3.85 (dd, 1H), 3.21 (m, 2H), 3.15(m, 2H), 3.01 (m, 2H), 1.98 (m, 2H), 1.90 (m, 2H), 1.84 (m, 2H), 1.78 (d, 3H) 1.72 (br, 1H).	511 [M+1]

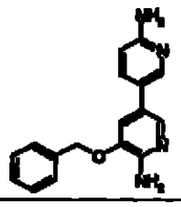
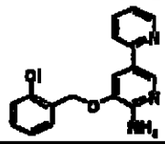
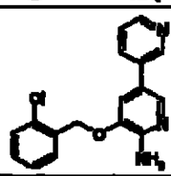
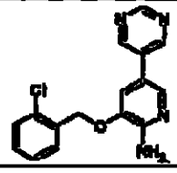
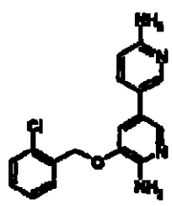
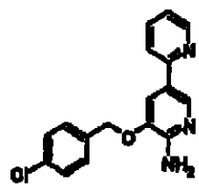
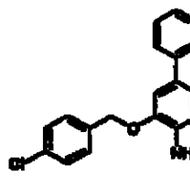
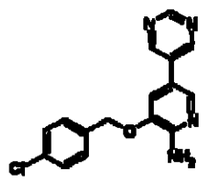
No.	Estructura	Nombre	Met IC_{20} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I-458		N- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- ilmetil}- metanosulfonamida	0% a 1uM		(400 MHz, DMSO- d_6) δ 7.51 (m, 1H), 7.43 (t, 2H), 7.28 (m, 1H), 6.70 (s, 1H), 5.96 (q, 1H), 5.68 (s, 2H), 3.84 (d, 2H), 2.68 (s, 3H), 1.76 (d, 3H)	409 [M+1]
I-459		N- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- ilmetil}- acetamida	2% a 1uM		(400 MHz, $CDCl_3$): d 7.49 (s, 1H), 7.29 (m, 1H), 7.06 (t, 1H), 6.71 (s, 1H), 6.03 (q, 1H), 5.49 (bs, 1H), 4.82 (bs, 2H) 4.29 (dd, 1H), 4.12 (dd, 1H), 1.96 (s, 3H), 1.83 (d, J 8.0 Hz, 3H).	372 [M+1]
I-460		N- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- ilmetil}- 4- metil- benzenosulfonamida	9% a 1uM		(400 MHz, $CDCl_3$): d 7.69 (d, 2H), 7.29 (m, 4H), 7.06 (t, 1H), 6.69 (s, 1H), 5.98 (q, 1H), 4.84 (bs, 2H), 4.51 (m, 1H), 3.86 (dt, 2H), 2.43 (s, 3H), 1.83 (d, J 8.0 Hz, 3H).	485 [M+1]
I-461		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- vinil- piridin- 2- ilamina	Hi 0.68		(400 MHz, $CDCl_3$): d 7.56 (s, 1H), 7.29 (m, 1 H), 7.05 (t, 1H), 6.91 (s, 1H), 6.19 (dd, 1H), 6.07 (q, 1H), 5.40 (d, J 16 Hz, 1H) 5.02 (d, J 12 Hz, 1H), 4.85 (bs, 2H), 1.85 (d, J 8.0 Hz, 3H).	327 [M+1]
I-462		(S)- 1- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- etano- 1,2- diol	2% a 1uM		(400 MHz, $CDCl_3$): d 7.55 (s, 1H), 7.29 (m, 1H), 7.05 (t, 1H), 6.82 (s, 1H), 6.05 (q, 1H), 4.82 (bs, 2H), 4.63 (m, 1H), 3.54 (m, 4H), 1.83 (d, J 8.0 Hz, 3H).	362 [M+1]
I-463		(R)- 1- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- etano- 1,2- diol	2% a 1uM		(400 MHz, $CDCl_3$): d 7.55 (s, 1H), 7.29 (m, 1H), 7,05 (t, 1H), 6.82 (s, 1H), 6.05 (q, 1H), 4.82 (bs, 2H), 4.63 (m, 1H), 3.54 (m, 4H), 1.83 (d, J 8.0 Hz, 3H).	362 [M+1]
I-464		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [1H- pirazol- 4- il)- piridin- 2- ilamina	HI 0.10		(400 MHz, $CDCl_3$): d 7.65 (s, 2H), 7.52 (s, 1H), 7.37 (m, 1H), 7.13 (m, 1H), 7.04 (s, 1H), 6.17 (q, J 8.0 Hz, 1H), 1.93 (d, J 8.0 Hz, 3H)	367 [M+1]
I-465		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [1- (2- pirrolidin- 1- il- etil)- 1H- pirazol- 4- il]- piridin- 2- ilamina	HI 0.34		(400 MHz, $CDCl_3$): d 7.71 (s, 1H), 7.55 (s, 2H), 7.37 (m, 1H), 7.06 (m, 1H), 6.87 (s, 1H), 6.09 (m, 1H), 4.26 (t, J 8.0 Hz, 2H), 2.96 (t, J 8.0 Hz, 2H), 2.55 (m, 4H), 1.87 (d, J 8.0 Hz, 3H), 1.26 (m, 4H)	465 [M+1]

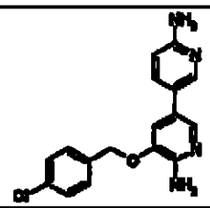
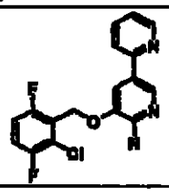
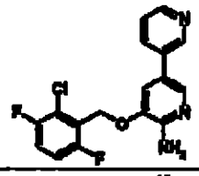
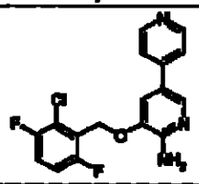
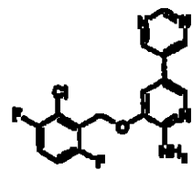
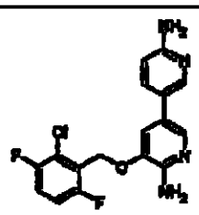
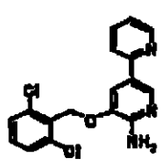
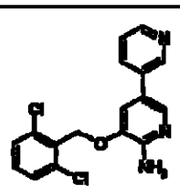
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 466		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [1- (2- diisopropilamino- etil)- 1H- pirazol- 4- il]- piridin- 2- ilamina	Hi 0.47		(400 MHz, $CDCl_3$): d 7.76 (s, 1H), 7.54 (s, 1H), 7.46 (s, 1H), 7.28 (m, 1H), 7.04 (m, 1H), 6.86 (m, 1H), 6.08 (m, 1H), 4.05 (t, J 8.0 Hz, 2H), 2.83 (t, 2H), 1.86 (d, J 4.0 Hz, 3H), 0.96 (d, J 8.0 Hz, 12H)	495 [M+1]
I- 467		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [1- (2- morfolin- 4- il]- piridin- 2- ilamina	Hi 0.083		(400 MHz, $CDCl_3$): d 7.72 (s, 1H), 7.60 (s, 1H), 7.50 (s, 1H), 7.38 (m, 1H), 7.13 (m, 1H), 7.05 (s, 1H), 6.19 (m, 1H) 4.61 (m, 2H), 3.89 (m, 4H), 3.53 (m, 2H), 3.02 (m, 4H), 1.93 (d, J 8.0 Hz, 3H).	481 [M+1]
I- 468		5- bromo- 3- (3- fluoro- 2- metoxi- benciloxi)- piridin- 2- ilamina	8% a 1uM		(400 MHz, DMSO- d_6) δ 7.67 (s, 1H), 7.43 (d, 1H), 7.40 (d, 1H), 7.33 (t, 1H), 7.20 (m, 1H), 6.00 (s, 2H) 5.19 (s, 2H), 3.96 (s, 3H)	328 [M+1]
I- 469		5- bromo- 3- [1- (3- fluoro- 2- metoxi- fenil)- etoxi]- piridin- 2- ilamina	7% a 1uM		(400 MHz, DMSO- d_6) δ 7.51 (s, 1H), 7.25 (d, 1H), 7.18 (m, 1H), 7.09 (m, 1H), 6.94 (s, 1H), 6.02 (s, 2H), 5.72 (q, 1H), 3.93 (s, 3H), 1.57 (d, 3H)	342 [M+1]
I- 470		[4- [6- amino- 5- (3- fluoro- 2- metoxi- benciloxi)- piridin- 3- il]- fenil)- ((3R,5S)- 3,5- dimetil- piperazin- 1- il)- metanona	3% a 1uM		(400 MHz, DMSO- d_6) δ 9.24 (s, 1H), 8.61 (d, 1H), 7.96 (d, 1H), 7.81 (d, 2H), 7.57 (d, 1H), 7.43 (d, 2H), 7.32 (t, 1H), 7.18 (m, 1H), 5.34 (s, 2H), 3.91 (s, 3H), 3.39 (m, 2H), 2.49 (m, 4H), 1.21(m, 6H).	465 [M+1]
I- 471		(4- [6- amino- 5- [1- (3- fluoro- 2- metoxi- fenil)- etoxi]- piridin- 3- il]- fenil)- ((3R,5S)- 3,5- dimetil- piperazin- 1- il)- metanona	1% a 1uM		(400 MHz, DMSO- d_6) δ 9.25 (d, 1H), 8.64 (d, 1H), 7.88 (s, 1H), 7.61 (d, 2H), 7.53 (d, 2H), 7.46 (s, 1H), 7.35 (d, 1H), 7.21 (t, 1H), 7.13 (m, 1H), 6.03 (m, 1H), 3.93 (s, 3H), 3.38 (m, 2H), 2.49 (m, 4H), 1.67 (d, 3H), 1.20 (m, 6H)	479 [M+1]

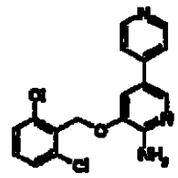
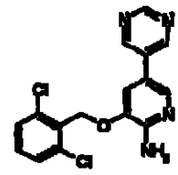
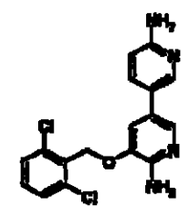
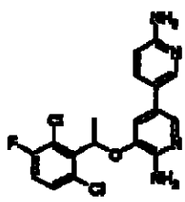
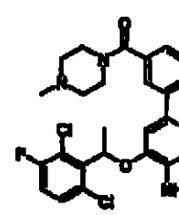
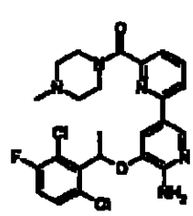
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 472		5- bromo- 3- (3- fluoro- 2- isopropoxi- benciloxi)- piridin- 2- ilamina	Hi 12.1		(400 MHz, DMSO- d_6) δ 7.59 (s, 1H), 7.36 (d, 1H), 7.31 (d, 1H), 7.25 (t, 1H), 7.12 (m, 1H) 5.90 (s, 2H), 5.10 (s, 2H), 4.43 (m, 1H), 1.26 (d, 6H)	356
I- 473		{4- [6- amino- 5- (3- fluoro- 2- isopropoxi- benciloxi)- piridin- 3- il]- fenil}- ((3R,5S)- 3,5- dimetil- piperazin- 1- il)- metanona	Hi 12.7		(400 MHz, DMSO- d_6) δ 9.45 (d, 1H), 8.79 (q, 1H), 7.99 (s, 1H), 7.88 (s, 1H), 7.80 (d, 2H), 7.58 (d, 2H), 7.41 (d, 1H), 7.32 (t, 1H), 7.17 (m, 1H), 5.37 (s, 2H), 4.45 (m, 1H), 3.40 (m, 2H), 2.49 (m, 4H), 1.28 (d, 8H), 1.20 (m, 6H)	493
I- 474		5- (4- amino- fenil- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina			(400 MHz, DMSO- d_6) δ 7.66 (d, 1 H), 7.55 (q, 1 H), 7.43 (t, 1H), 7.02 (d, 2H), 6.81 (s, 1H), 6.56 (d, 2H), 6.08 (q, 1H), 5.60 (s, 2H), 5.08 (s, 2H), 1.78 (d, 3H)	393
I- 475		metil ester del acido (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenoxi)- acetico	Hi 0.20		(400 MHz, $CDCl_3$): d 7.82 (s, 1H), 7.30 (m, 3H), 7.06 (m, 1H), 6.95 (m, 3H), 6.12 (q, 1H), 480 (m, 2H), 4.66 (s, 2H), 3.82 (s, 3H), 1.86 (d, J 8.0 Hz, 3H).	467
I- 476		acido (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenoxi)- acetico	Hi 0.20		(400 MHz, $CDCl_3$): d 7.70 (s, 1H), 7.50 (m, 2H), 7.45 (m, 2H), 7.20 (m, 2H), 6.85 (m, 2H), 6.05 (q, 1H), 5.72 (s, 2H), 4.49 (s, 2H), 3.82 (s, 3H), 1.75 (d, J 8.0 Hz, 3H).	453
I- 477		2- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenoxi)- 1- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- etanona	Hi 0.027	4	(400 MHz, $CDCl_3$): d 7.48 (s. 1H), 7.35 (m, 1H), 7.20 (m, 2H), 7.12 (m, 2H), 7.01 (m, 2H), 6.20 (q, 1H), 4.73 (m, 3H), 4.10 (m, 1H), 3.36 (m, 1H), 3.13 (m, 2H), 2.84 (m, 1H), 1.94 (d, J 8.0 Hz, 3H), 1.34 (m, 6H).	548

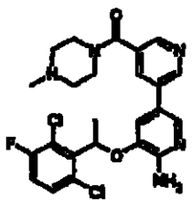
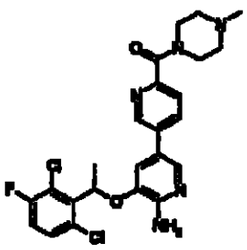
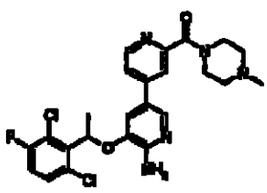
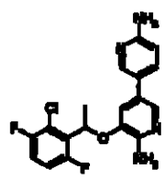
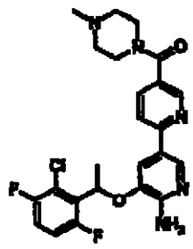
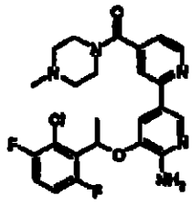
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I-478		2-(4-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-fenoxi)-1-((R)-3-hidroxi-pirrolidin-1-il)-etanona	HI 0.041	4	(400 MHz, $CDCl_3$): d 7.48 (s, 1H), 7.36 (m, 1 1I), 7.21 (d, 2H), 7.19 (m, 2H), 7.10 (m, 2H), 7.01 (m, 2H), 6.20 (q, 1H), 4.65 (m, 2H), 4.55 (m, 1H), 3.69 (m, 3H), 3.48 (m, 1H), 2.10 (m, 3H), 1.92 (m, 5H).	521
I-479		Terbutil éster del ácido 4-{2-(4-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-fenoxi)-acetil}-piperazina-1-carboxílico	Hi 0.16	4	(400 MHz, $CDCl_3$): d 7.50 (s, 1H), 7.36 (m, 1II), 7.22 (d, 2H), 7.19 (m, 2H), 7.15 (m, 2II), 7.00 (m, 2II), 6.20 (q, 1H), 4.75 (s, 2II), 3.57 (m, 4H), 3.45 (m, 4II), 1.93 (d, J 8.0 Hz, 3H), 1.47 (s, 9II)	620
I-480		2-(4-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-fenoxi)-1-((R)-2-pirrolidin-1-ilmetil-pirrolidin-1-il)-etanona		4	(400 MHz, $CDCl_3$): d 7.48 (s, 1H), 7.36 (m, 1H), 7.20 (d, 2H), 7,15 (m, 2H), 7.00 (d, 2H), 6.20 (q, 1H), 4.68 (s, 2H), 4.46 (m, 1H), 4.04 (m, 1II), 3.93 (m, 1H), 3.60 (m, 1H), 3.52 (m, 1H), 3.50 (m, 1II), 3.12 (m, 1H), 3.09 (m, 1II), 2.83 (m, 1H), 1.93 (d, J 8.0 Hz, 3H), 2.16-1.66 (m, 10H).	588
I-481		5-bromo-3-(3-fluoro-6,7,8,9-tetrahidro-5H-benzocicloheptano-5-iloxi)-piridin-2-ilamina		15	(400 MHz, DMSO-d_6) δ 7.57 (d, 1II), 7.16 (m, 3H), 6.95 (dt, 1II), 6.07 (d, 2H), 5.63 (d, 1II), 2.10 (m, 2H), 2.16 (m, 2H), 1.86 (m, 1H), 1.77 (m, 2H), 1.34 (m, 1H).	352
I-482		{4-[6-amino-5-(3-fluoro-6,7,8,9-tetrahidro-5H-benzocicloheptano-5-iloxi)-piridin-3-il]-fenil}-((3R,5S)-3,5-dimetil-piperazin-1-il)-metanona		3		493
I-483		3-(3-fluoro-6,7,8,9-tetrahidro-5H-benzocicloheptano-5-iloxi)-5-[4-(2-pirrolidin-1-il-etoxi)-fenil-piridin-2-ilamina		3		462

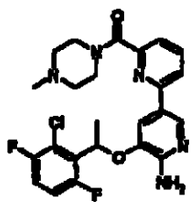
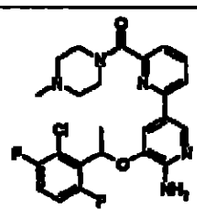
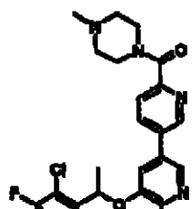
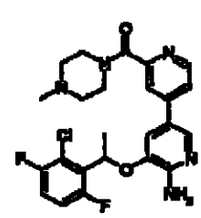
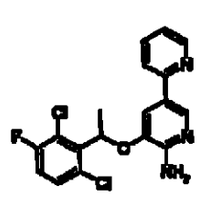
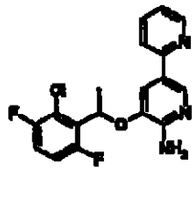
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I-484		N- {4- [6- amino- 5- (3- fluoro- 6, 7, 8, 9- tetrahidro- 5H- benzocicloheptano- 5- iloxi)- piridin- 3- il]- fenil}- metanosulfonamida				442
I-485		3- (3- fluoro- 6, 7, 8, 9- tetrahidro- 5H- benzocicloheptano- 5- iloxi)- 5- (1H- pirazol- 4- il)- piridin- 2- ilamina				337 [M- 1]
I-486		5- bromo- 3- [1- (2- cloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina	0% at 1uM		(400 MHz, $CDCl_3$): d 7.68 (s, 1H), 7.24 (m, 3H), 6.69 (s, 1H), 5.64 (q, 1H), 4.78 (bs, 2H), 1.68 (d, J 8.0 Hz, 3H).	347
I-487		3- [1- (2- cloro- 3- fluoro- fenil)- etoxi]- 5- [4- (2- pirrolidin- 1- il- etoxi)- fenil]- piridin- 2- ilamina	Hi 3.30		(400 MHz, $CDCl_3$): d 7.50 (s, 1H), 7.30 (m, 2H), 7.20 (m, 3H), 7.00 (s, 1H), 6.95 (m, 2H), 5.90 (q, 1H), 4.36 (m, 2H), 3.85 (m, 2H), 3.55 (m, 2H), 2.95 (m, 2H), 2.10 (m, 4H), 1.82 (d, J 8.0 Hz, 3H).	456
I-488		5'- benciloxi- [2,3']bipiridinil- 6'- ilamina	>20		($CDCl_3$) d 5.15 (br s, 2H), 5.19 (s, 2H), 7.17 (m, 1H), 7.34- 7.46 (m, 5H), 7.64 (d, J = 8 Hz, 1H), 7.70 (td, J = 7.8, 1.9 Hz, 1H), 7.86 (d, J = 1.6 Hz, 1H), 8.22 (d, J = 2 Hz, 1H), 8.63 (d, J = 4 Hz, 1H).	278
I-489		5- benciloxi- [3,3']bipiridinil- 6'- ilamina	>20		($CDCl_3$) d 5.17 (s, 2H), 5.27 (br s, 2H), 7.19 (d, J = 2 Hz, 1H), 7.33 (dd, J = 7.8, 4.6 Hz, 1H), 7.35- 7.44 (m, 5H), 7.70 (dt, J = 2,8 Hz, 1H), 7.85 (d, J = 2 Hz, 1H), 8.56 (dd, J = 1.6, 4.8 Hz, 1H), 8.71 (d, J = 2 Hz, 1H).	278
I-490		3- benciloxi- 5- pirimidin- 5- il- piridin- 2- ilamina	>20		($CDCl_3$) d 5.22 (s, 2H), 6.15 (br s, 2H), 7.21 (s, 1H), 7.43 (m, 5H), 7.77 (s, 1H), 8.81 (s, 2H), 9.20 (s, 1H).	279

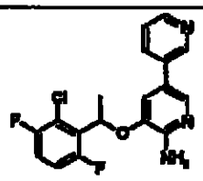
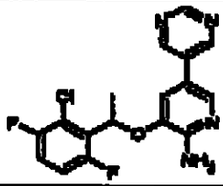
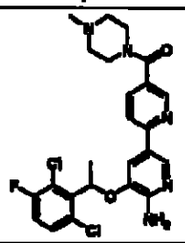
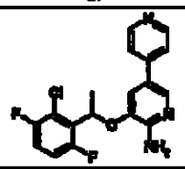
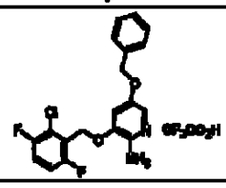
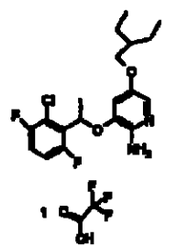
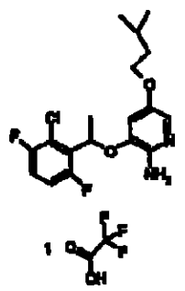
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 491		5- benciloxi- [3,3']bipiridinil- 6',6- diamina	>20		($CDCl_3$) d 4.40 (br s, 2H), 4.94 (br s, 2H), 5.13 (s, 2H), 6.58 (d, J = 8.4 Hz, 1H), 7.09 (d, J = 1.6 Hz, 1 H), 7.35- 7.44 (m, 5H), 7.56 (dd, J 2.4, 8.4 Hz, 1H), 7.77 (d, J 1.6 Hz, 1H), 8.13 (d, J = 2 Hz, 1H).	293
I- 492		5'- (2- cloro- benciloxi)- [2,3']bipiridinil- 6'- ilamina	8.24		($CDCl_3$) d 5.33 (s, 2H), 5.99 (bs, 2H), 7.22- 7.26 (m, 1H), 7.29- 7.37 (m, 2H), 7.42- 7.51 (m, 2H), 7.63 (d, 1H), 7.72 (dt, 1H), 7.99 (d, 1H), 8.13 (d, 1H), 8.65 (dd, 1H).	312
I- 493		5- (2- cloro- benciloxi)- [3,3']bipiridinil- 6'- ilamina	4.6			312
I- 494		3- (2- cloro- benciloxi)- 5- pirimidin- 5- il- piridin- 2- ilamina	19.3			313
I- 495		5- (cloro- benciloxi)- [3,3']bipiridinil- 6',6- diamina	4.31			317
I- 496		5'- (4- cloro- benciloxi)- [2,3']bipiridinil- 6'- ilamina	14		(CDCl3) d 5.18 (s, 2H), 5.48 (bs, 2H), 7.19- 7.22 (m, 1H), 7.38 (s, 4H), 7.63- 7.65 (m, 1H), 7.73 (dt, 1H), 7.89 (d, 1H), 8.17 (d, 1H), 8.63 (d, 1H).	312
I- 497		5- (4- cloro- benciloxi)- [3,3']bipiridinil- 6- ilamina	14.1			312
I- 498		3- (4- cloro- benciloxi)- 5- pirimidin- 5- il- piridin- 2- ilamina	>20.0			313

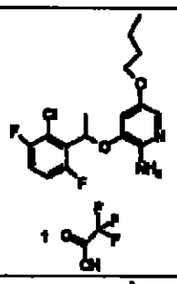
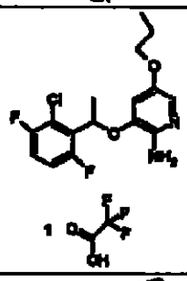
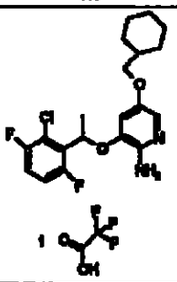
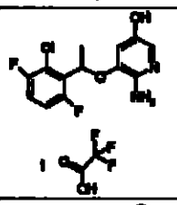
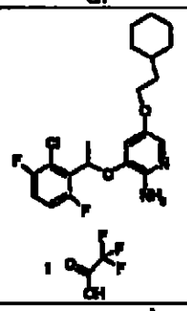
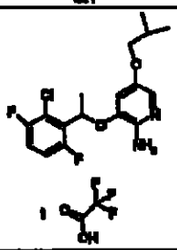
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 499		5- (4- cloro- benciloxi)- [3,3']bipiridinil- 6',6- diamina	>20.0			317
I- 500		5'- (2- cloro- 3,6- difluoro- benciloxi)- [2,3']bipiridinil- 6'- ilamina	1.8		(CDCl$_3$) δ 5.39 (s, 2H), 6.19 (bs, 2H), 7.08 (dt, 1H), 7.21- 7.28 (m, 2H), 7.65 (d, 1H), 7.77 (dt, 1H), 8.13 (d, 1H), 8.67 (dd, 1H)	348
I- 501		5- (2- cloro- 3,6- difluoro- benciloxi)- [3,3']bipiridinil- 6- ilamina	0.282			348
I- 502		5- (2- cloro- 3,6- difluoro- benciloxi)- [3,4']bipiridinil- 6- ilamina	0.211			348
I- 503		3- (2- cloro- 3,6- difluoro- benciloxi)- 5- pirimidin- 5- il- piridin- 2- ilamina	2.15			349
I- 504		5- (2- cloro- 3,6- difluoro- benciloxi)- [3,3']bipiridinil- 6,6'- diamina	0.209			363
I- 505		5'- (2,6- dicloro- benciloxi)- [2,3']bipiridinil- 6'- ilamina	2.84		(CDCl$_3$) d 5.47 (s, 2H), 5.76 (bs, 2H), 7.21- 7.25 (m, 1H), 7.27- 7.32 (m, 1H), 7.37- 7.41 (m, 2H), 7.66 (d, 1H), 7.75 (dt, 1H), 8.06 (d, 1H), 8.17 (d, 1H), 8.66 (dd, 1H).	346
I- 506		5- (2,6- dicloro- benciloxi)- [3,3']bipiridinil- 6- ilamina	2.71			346

No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 507		5- (2,6- dicloro- benciloxi)- [3,4']bipiridinil- 6- ilamina	1.3			346
I- 508		3- (2,6- dicloro- benciloxi)- 5 pirimidin- 5- il- piridin- 2- ilamina	10.3			347
I- 509		5- (2,6- dicloro- benciloxi)- [3,3']bipiridinil- 6,6'- diamina	0.578			361
I- 510		5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [3,3']bipiridinil- 6,6'- diamina	0.0167		(CDCl3) d 1.87 (d, J = 6.6 Hz, 3H), 4.60 (br s, 2H), 4.96 (br s, 2H), 6.11 (q, J = 6.6 Hz, 1H), 6.56 (d, J = 8.4 Hz, 1H), 6.91 (s, 1H), 7.06 (t, J = 8,5 Hz, 1H), 7.31 (dd, J = 4.8, 8.7 Hz, 1H), 7.48 (dd, J = 1.8, 8.4 Hz, 1H), 7.75 (s, 1H), 8.05 (s, 1H).	393
I- 511		{6'- amino- 5'- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [2,3']bipiridinil- 4- il}- (4- metil- piperazin- 1- il)- metanona	0.0742		(CDCl3) d 1.87 (d, 6.6 Hz, 3H), 2.37 (s, 3H), 2.39 (br s, 2H), 2.56 (br s, 2H), 3.43 (br s, 2H), 3.86 (br s, 2H), 5.13 (br s, 2H), 6.21 (q, J = 6.7 Hz, 1H), 7.04 (dd, J = 8.1, 8.7 Hz, 1H), 7.10 (dd, J = 1.2, 5.1 Hz, 1H), 7.29 (dd, J =5.1, 9.3 Hz, 1H), 7.48 (s, 1H), 7.57 (d, J = 1.5 Hz, 1H), 8.24 (d, J = 1.8 Hz, 1H) 8.65 (dd, J = 0.6, 4.8Hz, 1H).	504
I- 512		{6'- amino- 5'- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [2,3']bipiridinil- 6- il}- (4- metil- piperazin- 1- il)- metanona	0.0629		(CDCl$_3$) d 1.87 (d, J = 6.6 Hz, 3H), 2.36 (s, 3H), 2.46 (m, 2H), 2.58 (m, 2H), 3.66 (m, 2H), 3.89 (m, 2H), 5.08 (br s, 2H), 6.17 (q, J = 6.6 Hz, 1H), 7.05 (dd, J = 8.1, 8.8 Hz, 1H), 7.31 (dd, J = 5.0, 8.9 Hz, 1H), 7.46 (dd, J = 0.8, 7.7 Hz, 1H), 7.51 (dd, J = 1.8, Hz, 1H), 7.55 (dd, J = 0.8, 0.8 Hz, 1H), 7.76 (t, J = 7.5 Hz, 1H), 8.27 (d, J = 1.2 Hz, 1H).	504

No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I-513		{6'- amino- 5'- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [3,3']bipiridinil- 5- il}- (4- metil- piperazin- 1- il)- metanona	0.034		($CDCl_3$) d 1.88 (dd = 6.6 Hz, 3H), 2.38 (s, 3H), 2.44 (m, 2H), 2.56 (m, 2H), 3.52 (m, 2H), 3.87 (m, 2H), 5.05 (br s, 2H), 6.12 (q, J = 6.7 Hz, 1H), 6.97 (d, J = 1.8 Hz, 1H), 7.08 (dd, J = 8.1, 8.7 Hz, 7.33 (dd, J = 5.0, 8.9 Hz, 1H), 7.72 (t, J = 2.1 Hz, 1H), 7.86 (d, J = 2.1 Hz, 1H), 8.54 (d, J = 1.8 Hz, 1H), 8.65 d, J = 2.4 Hz, 1H).	504
I-514		{6'- amino- 5'- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [3,3']bipiridinil- 6- il}- (4- metil- piperazin- 1- il)- metanona	0.0213		($CDCl_3$): d 1.88 (d, J = 6.9 Hz, 3H), 2.39 (s, 3H), 2.52 (br s, 2H), 2.61 (br s, 2H), 3.74 (br s, 2H), 3.89 (br s, 2H), 5.02 (br s, 2H), 6.12 (q, J = 6.7 Hz, 1H), 6.97 (d, J = 1.2 Hz, 1H), 7.08 (t, J = 8.4 Hz, 1H), 7.33 (dd, J = 4.8, 8.7 Hz, 1H), 7.68 (d, J = 9 Hz, 1H), 7.76 (dd, J = 1.8, 8.4 Hz, 1H), 7.89 (d, J = 1.5 Hz, 1H), 8.59 (d, J = 1.5Hz, 1H).	504
I-515		{6'- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [3,4']bipiridinil- 2'- il}- (4- metil- piperazin- 1- il)- metanona	0.0387		($CDCl_3$): d 1.88 (d, J = 6.9 Hz, 3H), 2.39 (s, 3H), 2.51 (m, 2H), 2.61 (m, 2H), 3.67 (m, 2H), 3.90 (m, 2H), 5.08 (br s, 2H), 6.14 (q, J = 6.7 Hz, 1H), 7.05 (s, 1H), 7.06 (d, J = 7.8, 9 Hz, 1H), 7.32 (d, J = 5.1 Hz, 1H), 7.34 (dd, J = 5.0, 7.7Hz, 1H), 7.66 (d, J = 1.2 Hz, 1H), 8.00 (d, J = 1.8 Hz, 1H), 8.53 (d, J = 5.1 Hz, 1H).	504
I-516		5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [3,3']bipiridinil- 6,6'- diamina	0.0393		($CDCl_3$) d 1.83 (d, J = 6.6 Hz, 3H), 4.55 (br s, 2H), 4.87 (br s, 2H), 5.95 (q, J = 6.5 Hz, 1H), 6.55 (d, J = 8.4 Hz, 1H), 6.93- 7.12 (m, 3H), 7.48 (dd, J = 1.8, 8.4 Hz, 1H), 7.76 (s, 1H), 8.09 (s, 1H).	377
I-517		{6'- amino- 5'- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [2,3']bipiridinil- 5- il}- (4- metil- piperazin- 1- il)- metanona	0.131	16	($CDCl_3$) d 1.84 (d, J = 6.6 Hz, 3H), 2.39 (s, 3H), 2.53 (br s, 4H), 3.63 (br s, 2H), 3.82 (br s, 2H), 5.09 (br s, 2H), 6.06 (q, J = 6.5 Hz, 1H), 6.93- 7.10 (m, 2H), 7.60 (d, J = 7.8 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1 H), 7.76 (dd, J = 2.1, 8.4 Hz, 1H), 8.28 (d, J = 1.5 Hz, 1H), 8.66 (d, J = 1.5 Hz, 1H).	488
I-518		{6'- amino- 5'- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [2,3']bipiridinil- 4- il}- (4- metil- piperazin- 1- il)- metanona	0.209	16	($CDCl_3$) d 1.84 (d, J = 6.6 Hz, 3H), 2.40 (s, 3H), 2.45 (br s, 2H), 2.61 (br s, 2H), 3.48 (br s, 2H), 3.89 (br s, 2H), 5.13 (br s, 2H), 8.06 (q, J = 6.6 Hz, 1H), 6.93- 7.10 (m, 2H), 7.12 (dd, J = 1.2, 5.1 Hz, 1H), 7.52 (s, 1H), 7.68 (d, J = 1.2 Hz, 1H), 8.24 (d, J = 1.8 Hz, 1H), 8.67 (d, J = 4.8 Hz, 1H).	488

No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 519		{6'- amino- 5'- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [2,3']bipiridinil- 6- il}- (4- metil- piperazin- 1- il)- metanona	0.466	16	($CDCl_3$) d 1.84 (d, J = 6.6 Hz, 3H), 2.38 (s, 3H), 2.49 (m, 2H), 2.60 (m, 2H), 3.70 (m, 2H), 3.91 (m, 2H). 5.01 (br s, 2H), 6.02 (q, J = 6.6 Hz, 1H), 6.93- 7.12 (m, 2H), 7.49 (dd, J = 0.8, 7.7 Hz, 1H), 7.58 (dd, J = 0.9, 8.1 Hz, 1H), 7.62 (d, J = 1.8 Hz, 1H), 7.78 (t, J = 7.8 Hz, 1H), 8.29 (d, J = 1.8 Hz, 1 H)	488
I- 520		{6'- amino- 5'- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [3,3']bipiridinil- 5- il}- (4- metil- piperazin- 1- il)- metanona	0.134	16	($CDCl_3$) d 1.85 (d, J = 6.6 Hz, 3H), 2.44 (s, 3H), 2.57 (m, 4H), 3.59 (m, 2H), 3.91 (m, 2H), 5.02 (br s, 2H), 5.97 (q, J = 6.4 Hz, 1H), 6.96- 7.14 (m, 3H) 7.74 (s, 1H), 7.87 (br s, 1H), 8.57 (br s, 1H), 8.71 (br s, 1H).	488
I- 521		{6'- amino- 5'- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [2,3']bipiridinil- 6- il}- (4- metil- piperazin- 1- il)- metanona	0.0716	16	($CDCl_3$) d 1.86 (d, J = 6.6 Hz, 3H), 2.45 (s, 3H), 2.62 (br s, 2H), 2.69 (br s, 2H), 3.82 (br s, 2H), 3.95 (br s, 2H). 4.97 (br s, 2H), 5.98 (q, J = 6.5 Hz, 1H), 6.96- 7.14 (m, 3H), 7.71 (d, J = 8.1 Hz, 1H), 7.79 (dd, J = 2.3, 8.3 Hz, 1H), 7.90 (d, J = 2.1 Hz, 1H), 8.62 (d, J = 1.5 Hz, 1H).	488
I- 522		{6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [3,4']bipiridinil- 2'- il}- (4- metil- piperazin- 1- il)- metanona	0.0626	16	($CDCl_3$) d 1.86 (d, J = 6.6 Hz, 3H), 2.45 (s, 3H), 2.62 (br s, 2H), 2.70 (br s, 2H), 3.77 (br s, 2H), 3,96 (br s, 2H), 5.03 (br s, 2H), 5.99 (q, J = 6.7 Hz, 1H), 6.96- 7.14 (m, 2H), 7.16 (d, J = 1.8 Hz, 1H), 7.36 (dd, J = 2.0, 5.3 Hz, 1H), 7.71 (d, J = 1.2 Hz, 1H), 8.01 (d, J = 1.8 Hz, 1H), 8.45 (d, J = 4,8 Hz, 1H).	488
I- 523		5'- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [2,3']bipiridinil- 6- ilamina	0.0677	16	($CDCl_3$) d 1.87 (d, J = 6.6 Hz, 1H), 5.20 (br s, 2H), 6.23 (q, J = 6.7 Hz, 1H), 7.04 (t, J = 8.4 Hz, 1H), 7.15 (dd, J = 4.8, 6,6 Hz, 1H), 7.29 (dd, J = 5.1, 9.3 Hz, 1H), 7.51 (d, J = 8.1 Hz, 1H), 7.59 (d, J = 1.2 Hz, 1H), 7.67 (td, J = 7.8, 1.8 Hz, 1H), 8.24 (d, J = 1.5 Hz, 1H), 8.60 (d, J = 3.9 Hz, 1H).	378
I- 524		5'- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [2,3']bipiridinil- 6'- ilamina	0.612	16	($CDCl_3$) d 1.84 (d, J = 6.9 Hz, 3H), 5.14 (br s, 2H), 6.08 (q, J = 6.5 Hz, 1H), 6.93- 7.10 (m, 2H), 7.16 (dd, J = 5.1, 6.6 Hz, 1H), 7.54 (d, J = 8.1 Hz, 1H), 7.65- 7.70 (m, 2H), 8.24 (s, 1H), 8.62 (d, J = 4.2 Hz, 1H)	362

No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 525		5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [3,3']bipiridinil- 6- ilamina	0.0777	16	($CDCl_3$) d 1.87 (d, J = 6.6 Hz 3H), 5.37 (br s, 2H), 6.00 (q, J = 6.5 Hz, 1H), 6.97- 7.15 (m, 3H), 7.34 (dd, J = 4.7, 7.7 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1H), 7.82 (s, 1H), 8.56 (d, J = 3.9 Hz, 1H), 8.65 (s, 1H).	362
I- 526		3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- pirimidin- 5- il- piridin- 2- ilamina	0.552	16	($CDCl_3$) d 1.87 (d, J = 6.6 Hz, 3H), 5.16 (br s, 2H), 5.98 (q, J = 6.5 Hz, 1H), 6.96- 7.14 (m, 3H), 7.86 (s, 1H), 8.77 (s, 2H), 9.14 (s, 1H).	363
I- 527		{6'- amino- 5'- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [2,3']bipiridinil- 5- il}- (4- metil- piperazin- 1- il)- metanona	0.0385	16	($CDCl_3$) d 1.87 (d, J = 6.6 Hz, 3H), 2.38 (s, 3H), 2.51 (br s, 4H), 3.62 (br s, 2H), 3.81 (br s, 2H), 5.13 (br s, 2H), 6.21 (q, J = 6.7 Hz, 1H), 7.04 (t, J = 8.4 Hz, 1H), 7.30 (dd, J = 4.8, 8.7 Hz, 1H), 7.75 (dd, J = 1.9, 8.2 Hz, 1H), 8.28 (s, 1H), 8.64 (s, 1H).	504
I- 528		5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [3,4']bipiridinil- 6- ilamina	0.0659	16	($CDCl_3$) d 1.84 (d, J = 6 Hz, 3H), 5.13 (br s, 2H), 5.97 (q, J = 6.5 Hz, 1H), 6.95- 7.10 (m, 2H), 7.12 (d, J = 1.6 Hz, 1H), 7.30 (d, J = 6 Hz, 2H), 7.95 (d, J = 2 Hz, 1H), 8.58 (d, J = 5.6 Hz, 2H).	362
I- 529		5- benciloxi- 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 2- ilamina	2.58	17	($CDCl_3$) d 1.84 (d, 3H), 4.88 (s, 2H), 5.89 (q, 1H), 6.79 (d, 1H), 6.+1 (d, 1H), 7.01 (dt, 1H), 7.11, 7.17 (m, 1H), 7.28- 7.40 (m, 5H).	391
I- 530		3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- (2- etil- butoxi- piridin- 2- ilamina	4.08	17		385
I- 531		3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- (3- metil- butoxi- piridin- 2- ilamina	2.4	17		371

No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 532		3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- butoxi- piridin- 2- ilamina	1.94	17		357
I- 533		3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- propoxi- piridin- 2- ilamina	0.672	17		343
I- 534		3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- ciclohexilmetoxi- piridin- 2- ilamina	5.97	17		397
I- 535		6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- ol	0.54	17		301
I- 536		3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- (2- ciclohexil- etoxi)- piridin- 2- ilamina	7.5	17		411
I- 537		3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- isobutoxi- piridin- 2- ilamina	1.2	17		357

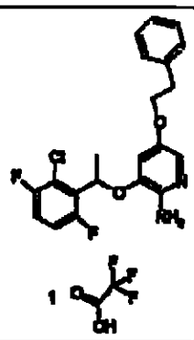
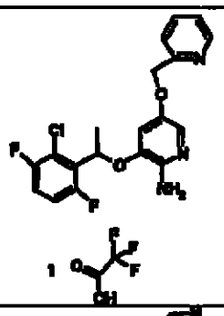
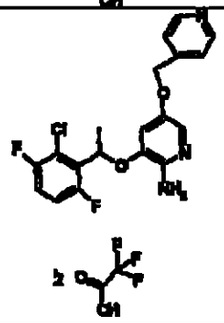
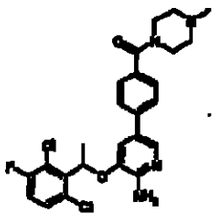
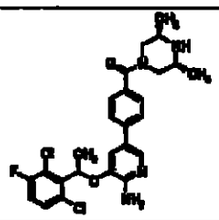
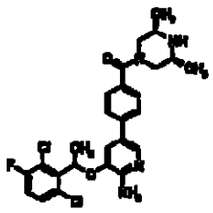
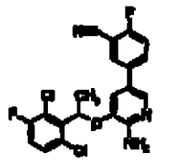
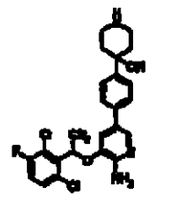
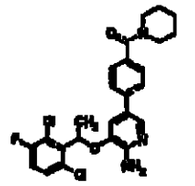
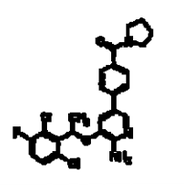
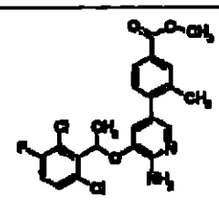
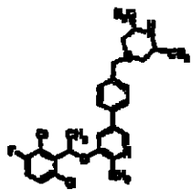
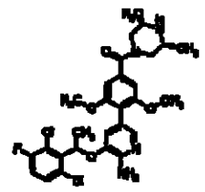
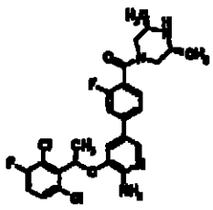
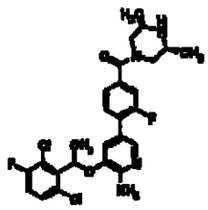
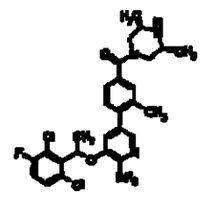
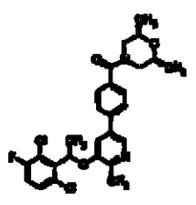
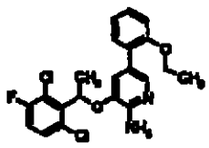
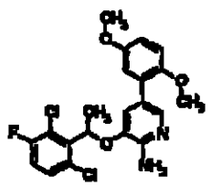
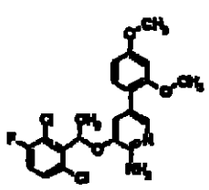
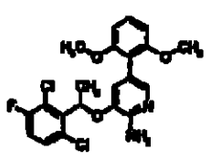
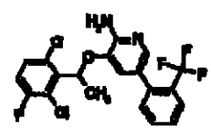
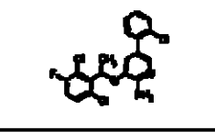
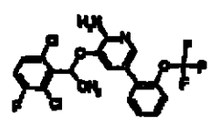
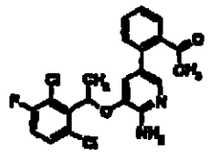
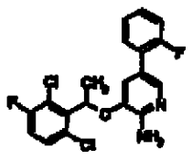
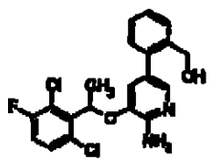
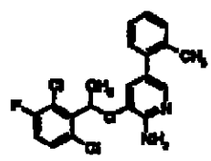
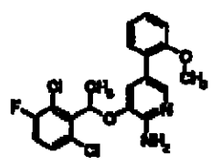
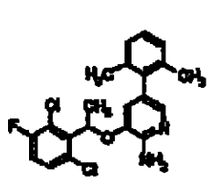
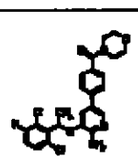
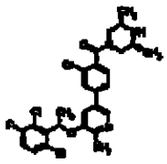
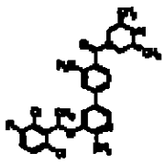
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
I- 538		3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- fenetiloxi- piridin- 2- ilamina	2.8	17		405
I- 539		3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- (piridin- 2- ilmetoxi)- piridin- 2- ilamina	3.2	17		392
I- 540		3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- (piridin- 4- ilmetoxi)- piridin- 2- ilamina	0.8	17		392
I- 541		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona	0.079	4 como en el ejemplo I- 291	(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.40 (m, 4H), 7.35 (dd, 1H), 7.08 (t, 1H), 7.02 (s, 1H), 6.17 (q, 1H), 4.98 (s, 2H), 3.82 (m, 2H), 3.62 (m, 2H), 2.52 (m, 4H), 1.88 (d, 3H).	567

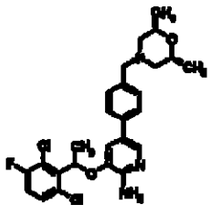
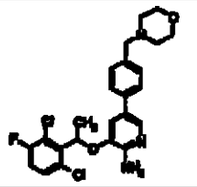
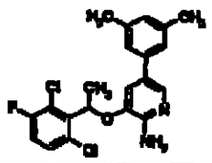
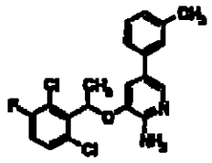
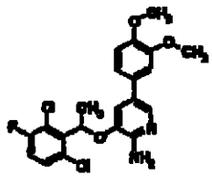
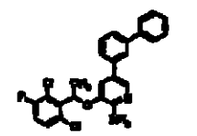
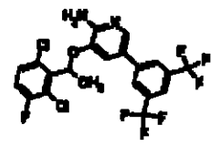
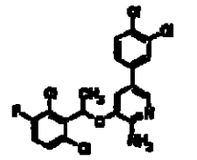
Tabla 3

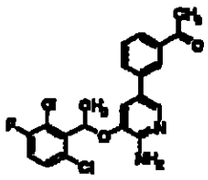
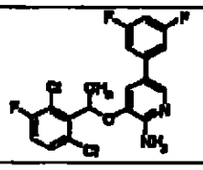
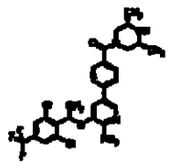
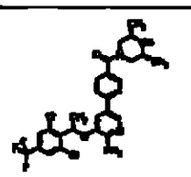
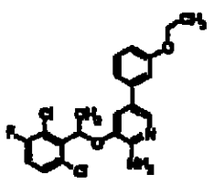
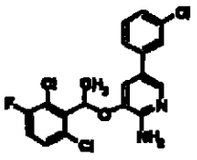
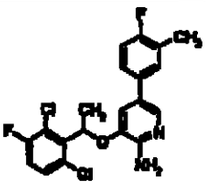
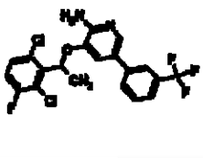
No.	Estructura	Nombre	Ki (μM) o I (%)	^{1}H- NMR	Ms m/z (M+H)	Procedimiento
I-542		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona	0.023	(400 MHz, DMSO- D_6) d ppm 0.84 (s, 3H) 0.93- 1.10 (m, 3H) 1.80 (d, J = 6.57 Hz, 3H) 2.30 (s, 2H) 2.55 - 2.74 (m, 2 H) 3.38 - 3.49 (m, 1H) 4.32 (s, 1H) 5.96 (s, 2H) 6.14 (q, J = 6.57 Hz, 1H) 7.00 (d, J = 1.77 Hz, 1 H) 7.36 (m, 2H) 7.45 (m, 3H) 7.56 (dd, J = 8.97, 4.93 Hz, 1H) 7.88 (d, J = 1.77 Hz, 1H)	517	18/19/ 20/31
I-543		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona	1.5	(400 MHz, DMSO- D_6) d ppm 0.84 (s, 3H) 0.93- 1.10 (m, 3H) 1.80 (d, J = 6.57 Hz, 2H) 2.30 (s, 2H) 2.55 - 2.74 (m, 2H) 3.38 - 3.49 (m, 1H) 4.32 (s, 1H) 5.96 (s, 2H) 6.14 (q, J = 6.57 Hz, 1H) 7.00 (d, J = 1.77 Hz, 1H) 7.36 (m, 2H) 7.45 (m, 3H) 7.56 (dd, J = 8.97, 4.93 Hz, 1H) 7.88 (d, J = 1.77 Hz, 1H)	517	18/19/ 20/31
I-544		5- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 2- fluoro- benzonitrilo		(400 MHz, DMSO- D_6) d ppm 1.80 (d, J = 6.82 Hz, 3H) 6.01 (s, 2H) 6.17 (q, J = 6.57 Hz, 1H) 7.05 (d, J = 1.77 Hz, 1H) 7.44 (t, J = 8.72 Hz, 1H) 7.55 (m, 2H) 7.79 (m, 1H) 7.89 (d, J = 1.77 Hz, 1 H) 7.97 (dd, J = 6.06, 2.27 Hz, 1H)	420	27
I-545		4- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- piperidin- 4- ol		(400 MHz, DMSO- D_6) d ppm 1.49- 1.65 (m, 2H) 1.75 - 1.86 (m, 3H) 1.86 - 1.98 (m, 3H) 2.53 (s,1H) 2.88 (s, 2H) 2.99 (s, 2H) 5.84 (s, 2H) 6.11 (d, J = 6.57 Hz, 1H) 6.93 (s, 1H) 7.28 - 7.38 (m, J = 8.08 Hz, 2H) 7.39 - 7.50 (m, J = 8.21, 8.21 Hz, 3H) 7.57 (dd, J = 8.72, 4.93 Hz, 1H) 7.81 (s, 1H)	477	27
I-546		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- piperidin- 1- il)- metanona	0.057	(400 MHz, DMSO- D_6) d ppm 1.43 - 1.56 (m, 4H) 1.61 (d, J = 3.79 Hz, 4H) 1.81 (d, J = 6.57 Hz, 3H) 3.51 (s, 2H) 5.94 (s, 2H) 6.15 (d, J = 6.82 Hz, 1H) 7.00 (d, J = 1.77 Hz, 1H) 7.28- 7.41 (m, 2H) 7.40 - 7.50 (m, 3H) 7.57 (dd, J = 9.09, 5.05 Hz, 1H) 7.87 (d, J = 2.02 Hz, 1H)	488	20
I-547		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- pirrolidin- 1- il)- metanona	0.067	(400 MHz, DMSO- D6) d ppm 1.73 - 1.93 (m, 7H) 3.39 - 3.52 (m, 4H) 5.96 (s, 2H) 6.07 - 6.20 (m, J = 6.82 Hz, 1H) 6.99 (d, J = 1.77 Hz, 1H) 7.39 - 7.47 (m, 3H) 7.52 (d, 2H) 7.56 (dd, J = 9.09, 5.05 Hz, 1H) 7.82 - 7.92 (m, J = 1.77 Hz, 1H)	474	20
I-548		Ester metil del acido 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- metil- benzoico	17%	(400 MHz, CLOROFORMO- D) d ppm 1.77 - 1.88 (m, 3H) 2.11 (s, 3H) 3.91 (s, 3H) 4.90 (s, 2H) 6.02 (d, J = 6.82 Hz, 1H) 6.69 (d, J = 1.77 Hz, 1H) 7.00- 7.09 (m, 1H) 7.14 (d, J = 7.83 Hz, 1H) 7.26 - 7.31 (m, 1H) 7.59 (d, J = 1.77 Hz, 1H) 7.83 (dd, J = 7.96, 1.39 Hz, 1H) 7.88 (s, 1H)	450	19

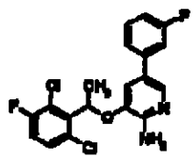
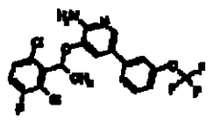
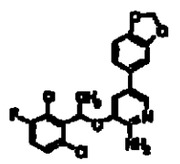
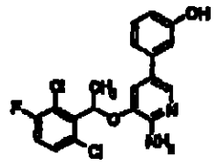
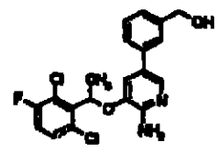
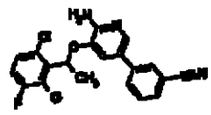
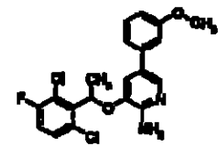
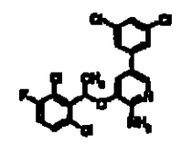
No.	Estructura	Nombre	Ki (μM) o I (%)	^{1}H- NMR	Ms m/z (M+H)	Procedimiento
I-549		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [4- (dimetil- piperazin- 1- ilmetil)- fenil]- piridin- 2- ilamina	0.095	(400 MHz, DMSO- D_6) d ppm 0.84 - 0.96 (m, 6H) 1.44- 1.61 (m, 2H) 1.72- 1.83 (m, 3H) 2.58- 2.70 (m, 2H) 2.71- 2.84 (m, 4H) 5.76- 5.92 (m, 2H) 6.02- 6.18 (m, 1H) 6.88 - 7.01 (m, 1H) 7.25 (d, 2H) 7.32 (d, 2H) 7.38- 7.49 (m, 1H) 7.50- 7.64 (m, 2H) 7.76- 7.88 (m, 1H)	503	28
I-550		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 3,5- dimetoxi- fenil)- (dimetil- piperazin- 1- il)- metanona	15%	(400 MHz, DMSO- D_6) d ppm 0.77- 0.91 (m, 3H) 1.00 (s, 3H) 1.75 (d, J = 6.82 Hz, 3H) 2.16- 2.30 (m, J = 12.63 Hz, 3H) 2.64- 2.76 (m, 3H) 3.54 (s, 6H) 4.25- 4.40 (m, 1H) 5.69 (s, 2H) 5.91 (q, J = 6.74 Hz, 1H) 6.54- 6.67 (m, 3H) 7.37- 7.43 (m, 1H) 7.43 - 7.51 (m, 1H) 7.51- 7.60 (m, 1H)	577	19/20
I-551		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 2- fluoro- fenil)- (dimetil- piperazin- 1- il)- metanona	0.091	(400 MHz, DMSO- D_6) d ppm 0.80- 0.96 (m, 3H) 1.06 (s, 3H) 1.80 (d, J = 6.57 Hz, 3H) 2.26- 2.42 (m, J = 1.52 Hz, 2H) 2.61- 2.85 (m, J = 1.77 Hz, 3H) 4.35- 4.47 (m, J = 6.32 Hz, 1H) 6.06 (s, 2H) 6.16 (q, J = 6.57 Hz, 1H) 7.02 (s, 1H) 7.27- 7.40 (m, 3H) 7.40- 7.49 (m, J = 8.72, 8.72 Hz, 2H) 7.51- 7.62 (m, J = 8.84, 5.05 Hz, 1H) 7.93 (s, 1H)	535	19/20
I-552		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 3- fluoro- fenil)- (dimetil- piperazin- 1- il)- metanona	0.2237	(400 MHz, DMSO- D_6) d ppm 0.83 - 1.00 (m, 3H) 1.02 - 1.17 (m, 3H) 1.78 (d, 3H) 2.70 - 2.98 (m, 6H) 4.36 - 4.50 (m, 1H) 6.01- 6.10 (m, 2H) 6.10 - 6.22 (m, 1H) 6.96- 7.04 (m, 1H) 7.06 - 7.15 (m, 1H) 7.16 - 7.23 (m, 1H) 7.30 - 7.39 (m, 1H) 7.40 - 7.49 (m, 1H) 7.50 - 7.59 (m, 1H) 7.86 - 7.98 (m, 1H)	535	19/20
I-553		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 3- metil- fenil)- (dimetil- piperazin- 1- il)- metanona	0.2593	(400 MHz, DMSO- D_6) d ppm 0.88 (s, 3H) 1.01 (s, 3H) 1.77 (d, J = 6.57 Hz, 3H) 1.96 (s, 3H) 2.31 (s, 1H) 2.73 (s, 3H) 3.50 (s, 2H) 4.35 (s, 1H) 5.89 (s, 2H) 6.00 (q, J = 6.57 Hz, 1H) 6.60 (s, 1H) 7.01- 7.12 (m, J = 7.83Hz 1H) 7.12 - 7.28 (m,2H) 7.37 - 7.63 (m, 3H)	531	19/20
I-554		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((2R,6S)- 2,6- dimetil- morfolin- 4- il)- metanona	0.1407	(400 MHz, DMSO- D_6) d ppm 1.00 - 1.31 (m, 4H) 1.87 (d, J = 6.82Hz, 3H) 3.37 - 3.40 (m, 6H) 3.55- 3.65 (m, 2H) 6.01 - 6.05 (m, 2H) 6.21 (q, J = 6.57 Hz, 1H) 7.07 (d, J = 1.77 Hz, 1H) 7.45 - 7.55 (m, 5H) 7.63 (dd, J = 8.84, 5.05 Hz, 1H) 7.92 - 7.98 (m, 1H)	518	19

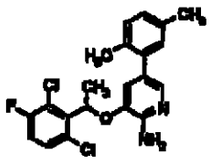
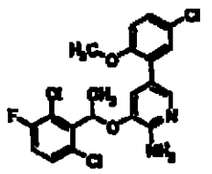
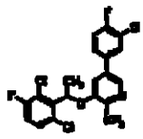
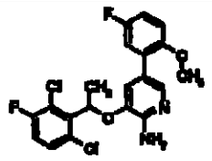
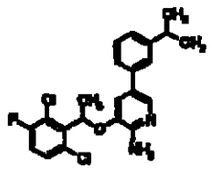
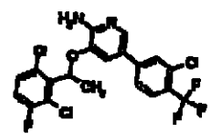
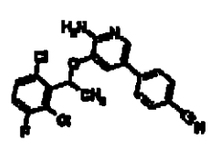
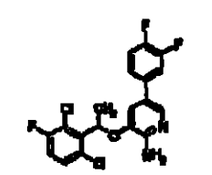
No.	Estructura	Nombre	KI (μM) o I (%)	^{1}H- NMR	Ms m/z (M+H)	Procedimiento
I-555		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2- etoxi- fenil)- piridin- 2- ilamina	22%	(400 MHz, DMSO- D_6) d ppm 1.36 (t, J = 6.82Hz, 3H) 1.95 (d, J = 6.57 Hz, 3H) 4.08 - 4.16 (m, 2H) 5.91 – 5.95 (m, 2H) 6.16 (q, J = 6.57 Hz, 1H) 7.08 - 7.13 (m, 2H) 7.19 (d, J = 7.83Hz, 1H) 7.27 (d,d, J = 7.58, 1.77 Hz, 1H) 7.40 (t, J = 8.59 Hz, 1H) 7.62 (t, J = 8.59 Hz, 1H) 7.73 (dd, J = 9.09, 5.05 Hz, 1H) 7.84 (d, J = 1.77 Hz, 1H)	421	19
I-556		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,5- dimetoxi- fenil)- piridin- 2- ilamina	0.5746	(400 MHz, DMSO- D_6) d ppm 1.82 (d, J = 6.57 Hz, 3H) 3.57 - 3.58 (m, 3H) 3.74 - 3.75 (m, 3H) 5.82- 5.86 (m, 2H) 6.03 (q, J = 6.57 Hz, 1H) 6.72 (d, J = 3.28 Hz, 1H) 6.84 (dd, J = 8.84, 3.03Hz, 1H) 6.89 (d, J = 1.77 Hz, 1H) 6.98 (d, J = 9.09 Hz, 1H) 7.50 (t, J = 8.59 Hz, 1H) 7.61 (dd, J = 8.84, 4.80 Hz, 1H) 7.66 (d, J = 1.77 Hz, 1H)	437	19
I-557		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,4- dimetoxi- fenil)- piridin- 2- ilamina	0.2172	(400 MHz, DMSO- D_6) d ppm 1.83 (d, J = 6.82Hz, 3H) 3.64 - 3.67 (m, 3H) 3.81 - 3.84 (m, 3H) 5.74 - 8.78 (m, 2H) 6.03 (q, J = 6.57 Hz, 1H) 6.59 (dd, J = 8.34, 2.27 Hz, 1H) 6.64 (d, J = 2.53 Hz, 1H) 6.88 (d, J = 1.77 Hz, 1H) 7.10 (d, J = 8.34 Hz, 1H) 7.53 (t, J = 8.59 Hz, 1H) 7.58(d, J = 1.77 Hz, 1H) 7.63 (d,d, J = 8.84, 5.05 Hz, 1H)	437	19
I-558		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,6- dimetoxi- fenil)- piridin- 2- ilamina	2%	(400 MHz, DMSO- D_6) d ppm 1.81 (d, J = 6.82 Hz, 3H) 3.58 - 3.59 (m, 6 H) 5.68 - 5.69 (m, 2H) 5.96 (q, J = 6.82 Hz, 1H) 6.63 (d, J = 1.77 Hz, 1H) 6.71 (d, J = 8.34 Hz, 2H) 7.26 (t, J = 8.34 Hz, 1H) 7.42 (d, J = 1.52 Hz, 1H) 7.52 (t, J = 8.59 Hz, 1H) 7.61 (dd, J = 8.84, 5.05 Hz, 1H)	437	19
I-559		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2- trifluorometil- fenil)- piridin- 2- ilamina	4%	(400 MHz, DMSO- D_6) d ppm 1.78 (d, J = 6.57 Hz, 3H) 5.91 - 5.99 (m, 3H) 6.59 - 6.60 (m, 1H) 7.26 (d, J = 7.58 Hz, 1H) 7.42 - 7.48 (m, 2H) 7.50 - 7.58 (m, 2H) 7.65 (t, J = 7.33 Hz, 1H) 7.75 (d, J = 7.83 Hz, 1H)	445	19
I-560		3- (2- cloro- fenil)- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina	24%	(400 MHz, DMSO- D_6) d ppm 1.79 (d, J = 6.82 Hz, 3H) 5.96 - 6.03 (m, 3H) 6.75 (d, J = 1.77 Hz, 1H) 7.27 - 7.38 (m, 3H) 7.42 - 7.49 (m, 2H) 7.52 - 7.57 (m, 2H)	411	19
I-561		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2- trifluorometoxi- fenil)- piridin- 2- ilamina	14%	(400 MHz, DMSO- D_6) d ppm 1.74 (d, J = 6.82 Hz, 3H) 5.92 - 5.98 (m, 3H) 6.74 (d, J = 1.77 Hz, 1H) 7.29 - 7.43 (m, 5H) 7.50 (dd, J = 9.09, 5.05 Hz, 1H) 7.56 (d, J = 1.77 Hz, 1H)	461	19
I-562		1- (2- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- etanona	8%	(400 MHz, DMSO- D_6) d ppm 1.83 (d, J = 6.82 Hz, 3H) 1.92 - 1.93 (m, 3H) 6.01 - 6.07 (m, 3H) 6.59 (d, J = 2.02 Hz, 1H) 7.26 (d, J = 7.83 Hz, 1H) 7.45 (t, J = 7.33 Hz, 1H) 7.48 - 7.51 (m, 1H) 7.52 - 7.58 (m, 3H) 7.61 (dd, J = 8.84, 5.05 Hz, 1H)	419	19

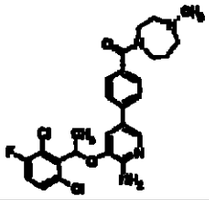
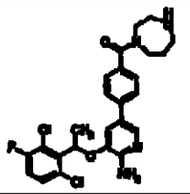
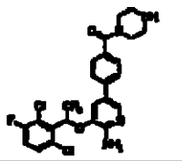
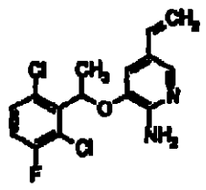
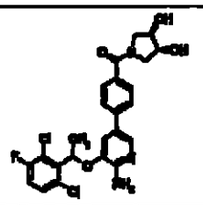
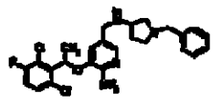
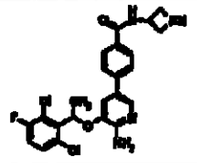
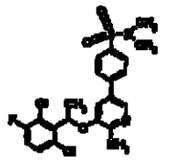
No.	Estructura	Nombre	Ki (μM) o I (%)	^{1}H- NMR	Ms m/z (M+H)	Procedimiento
I-563		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2- trifluorometoxi- fenil)- piridin- 2- ilamina	0.4322	(400 MHz, DMSO- D_6) d ppm 1.71 (d, J = 6.57 Hz, 3H) 5.88 - 5.90 (m, 2H) 5.96 (q, J = 6.82 Hz, 1H) 6.76 - 6.78 (m, 1H) 7.10 - 7.16 (m, 2H) 7.19 - 7.28 (m, 2H) 7.36 (t, J = 8.59 Hz, 1H) 7.47 (dd, J = 8.84, 4.80 Hz, 1H) 7.60 - 7.63 (m, 1H)	395	19
I-564		(2- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- metanol	21%	(400 MHz, DMSO- D_6) d ppm 1.79 (d, J = 6.57 Hz, 3H) 4.20 (t, J = 5.05 Hz, 2H) 5.03 (t, J = 5.56 Hz, 1H) 5.82 - 5.83 (m, 2H) 6.02 (q, J = 6.57 Hz, 1H) 6.68 (d, J = 1.77 Hz, 1H) 7.01 (dd, J = 7.58, 1.52 Hz, 1H) 7.31 (dt, J = 7.33, 1.26 Hz, 1H) 7.46 (t, J = 8.59 Hz, 1H) 7.49 - 7.53 (m, 2H) 7.56 (dd, J = 8.84, 5.05 Hz, 1H)19	407	19
I-565		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- o- tolil- piridin- 2- ilamina	25%	(400 MHz, DMSO- D_6) d ppm 1.65 (d, J = 6.57 Hz, 1H) 1.80 - 1.80 (m, 3H) 5.67 - 5.69 (m, 2H) 5.86 (q, J = 6.57 Hz, 1H) 6.45 (d, J = 1.77 Hz, 1H) 6.86 - 6.90 (m, 1H) 7.00 - 7.09 (m, 3H) 7.29 - 7.35 (m, 2H) 7.42 (dd, J = 8.84, 5.05 Hz, 1H)	391	19
I-566		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2- metoxi- fenil)- piridin- 2- ilamina	0.2779	(400 MHz, DMSO- D_6) d ppm 1.84 (d, J = 6,57 Hz, 3H) 3.65 - 3.66 (m, 3H) 5.83 - 5.84 (m, 2H) 6.04 (q, J = 6.57 Hz, 1H) 0.93 (d, J= 1.77 Hz, 1H) 7.00 (dt, J = 7.33, 1.01 Hz, 1H) 7.08 (d, J = 7.83 Hz, 1H) 7.19 (dd, J = 7.58, 1.77 Hz, 1H) 7.28 - 7.34 (m, 1H) 7.53 (t, J = 8.84 Hz, 1H) 7.61 - 7.66 (m, 2H)	407	19
I-567		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,6- dimetil- fenil)- piridin- 2- ilamina	0%	(400 MHz, DMSO- D_6) d ppm 1.57 - 1.58 (m, 3H) 1.79 (d, J = 6.82 Hz, 3H) 1.97 - 1.98 (m, 3H) 5.73 - 575 (m, 2H) 5.98 (q, J = 6.57 Hz, 1H) 6.41 (d, J = 1.77 Hz, 1H) 6.99- 7.11 (m, 3H) 7.25 (d, J = 1.77 Hz, 1H) 7.44 (t, J = 8.59 Hz, 1H) 7.54 (dd, J = 8.84, 5.05 Hz, 1H)	405	19
I-568		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- morfolin- 4- il- metanona	0.0525	Anal. Calcd para C24 H22 Cl2 F N3 O3: C, 58.79; H, 4.52; N, 8.57. Encontrados: C, 58.39; H, 4.72; N, 8.24.	490	20
I-569		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 2- cloro- fenil)- ((3R, 5S)- dimetil- piperazin- 1- il)- metanona	0.0478	Anal, Calcd para C26 H26 Cl3 F N4 O2: C, 56.59; H, 4.75; N, 10.15. Encontrados: C, 52.83; H, 5.16; N, 8.79. 1.1 eq de H20; 1.3 eq AcOH	551	19/20
I-570		4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 2- metil- fenil)- ((3R, 5S)- dimetil- piperazin- 1- il)- metanona	0.225	Anal. Calcd for C27 H29 Cl2 F N4 O2: C, 61.02; H, 5.50; N, 10.54. Encontrados: C, 55.99; H, 5.79; N, 9.01. 1.2 eq de H20; 1.5 eq de AcOH	531	19/20

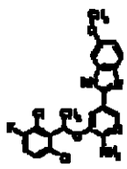
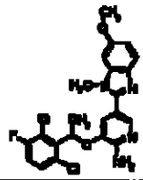
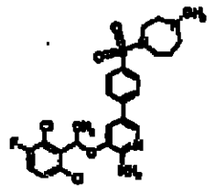
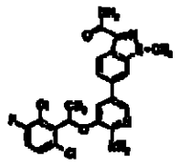
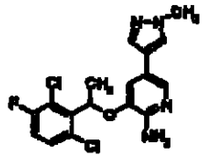
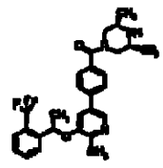
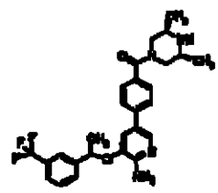
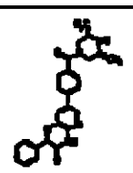
No.	Estructura	Nombre	Ki (μM) o I (%)	^{1}H- NMR	Ms m/z (M+H)	Procedimiento
I-571		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [4- ((2R, 6S)- 2,6- dimetil- morfolin- 4- ilmetil)- fenil]- piridin- 2- ilamina	0.2204	(4011 MHz, CLOROFORMO- D) d ppm 1.09 (d, J = 6.32 Hz, 6H) 1.80 d, J = 6.82 Hz, 3H) 1.88 - 1.98 (m, 2H) 2.78 - 2.90 (m, 2H) 3.59 – 3.70 (m, 2H) 3.86 - 3.95 (m, 2H) 5.12 - 5.16 (m, 2H) 6.06 (q, J = 6.57 Hz, 1H) 6.94 - 7.04 (m, 2H) 7.25 (dd, J = 8.84, 4.80 Hz, 1H) 7.28 - 7.34 (m, 2H) 7.36 - 7.44 (m, 2H) 7.77 (d, J = 1.52 Hz, 1H)	504	28
I-572		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (4- morfolin- 4- ilmetil)- fenil)- piridin- 2- ilamina	0.0554	(400 MHz, CLOROFORMO- D) d ppm 1.80 (d, J = 6,57 Hz, 3H) 2.51 - 2.58 (m, 4H) 3.58 - 3.60 (m, 2H) 3.75 (t, J = 4.55 Hz, 4 H) 5.27 - 5.31 (m, 2H) 6.06 (q, J = 6.57 Hz, 1H) 6.95 (d, J = 1.52 Hz, 1H) 7.00 (t, J = 8.08 Hz, 1H) 7.22 - 7.29 (m, 3H) 7.33 - 7.37 (m, 2H) 7.74 (d, J = 1.77 Hz, 1H)	476	28
I-573		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3,5- dimetil- fenil)- piridin- 2- ilamina		(400 MHz, DMSO- D_6) d ppm 1.64 (d, J = 6.57 Hz, 3H) 2.08 - 2.10 (m, 6H) 5.65 - 5.68 (m, 2H) 5.93 (q, J= 6.57 Hz, 1H) 6.69- 6.71 (m, 2H) 6.75 - 6.78 (m, 2H) 7.28 (t, J = 8.59 Hz, 1H) 7.40 (dd, J = 9.09, 4.80 Hz, 1H) 7.62 (d, J = 1.77 Hz, 1H)	405	19
I-574		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- m- tolil- piridin- 2- ilamina		(400 MHz, DMSO- D_6) d ppm 1.78 (d, J = 6,57 Hz, 3H) 2.27 - 228 (m, 3H) 5.80 - 5.84 (m, 2H) 6.08 (q, J = 6.57 Hz, 1H) 6.88 (d, J = 1.77 Hz, 1H) 7.02 (d, J = 7.33 Hz, 1H) 7.09 - 7.15 (m, 2H) 7.21 (t, J = 7.58 Hz, 1H) 7.41 (t, J = 8.59 Hz, 1H) 7.54 (dd, J = 9.9, 5.05 Hz, 1H) 7.77 (d, J = 1.77 Hz, 1H)	391	19
I-575		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3,4- dimetoxi- fenil)- piridin- 2- ilamina		(400 MHz, DMSO- D_6) d ppm 1.60 (d, J = 6.57 Hz, 3H) 3.55 (d, J = 14.91 Hz, 6 H) 5.57 - 5.60 (m, 2H) 5.90 (q, J = 6.57 Hz, 1H) 6.83 (d, J = 2.02 Hz, 1H) 6.65 (d, J = 1.77 Hz, 1H) 6.68 - 6.76 (m, 2H) 7.23 (t, J = 8.59 Hz, 1H) 7.36 (dd, J = 4.80, 4.04 Hz, 1H) 7.58 (d, J = 1.77 Hz, 1H)	437	19
I-576		5- bifenil- 3- il- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina		(400 MHz, DMSO- D_6) d ppm 1.83 (d, J = 6.57 Hz, 3H) 5.92 - 5.95 (m, 2H) 6.16 (q, J = 6,57 Hz, 1H) 7.01 (d, J = 1.52 Hz, 1H) 7.38 – 7.59 (m, 9H) 7.69 (d, J = 7.33 Hz, 2H) 7.93 (d, J = 1.52 Hz, 1H)	453	19
I-577		3- (3,5- bis- trifluorometil- fenil)- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina		(400 MHz, DMSO- D_6) d ppm 1.84 (d, J = 6.57 Hz, 3H) 6.16 - 6.24 (m, 3H) 7.03 (d, J = 1.77 Hz, 1H) 7.45 (t, J = 8.59 Hz, 1H) 7.54 (dd, J = 9.09, 5.05 Hz, 1H) 7.92 - 7.95 (m, 1H) 8.00 – 8.02 (m, 2H) 8.08 (d, J = 2.02 Hz, 1H)	513	19
I-578		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3,4- dicloro- fenil)- piridin- 2- ilamina		(400 MHz, DMSO- D_6) d ppm 1.87 (d, J = 6.57 Hz, 3H) 6.09- 6.12 (m, 2H) 6.22 (q, J = 6.57 Hz, 1H) 7.04 (d, J = 1.77 Hz, 1H) 7.46 - 7.53 (m, 2H) 7.62 (dd, J = 9.09, 5.05 Hz, 1H) 7.66 - 7.70 (m, 2H) 7.96 (d, J = 2.02 Hz, 1H)	446	19

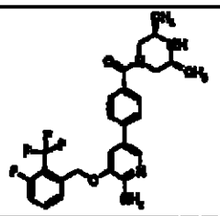
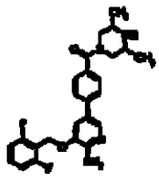
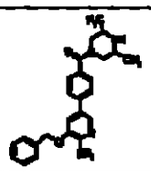
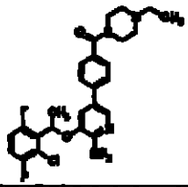
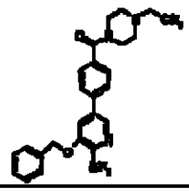
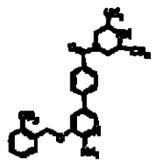
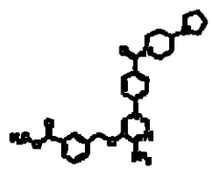
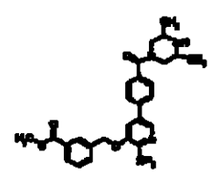
No.	Estructura	Nombre	Ki (μM) o I (%)	^{1}H- NMR	Ms m/z (M+H)	Procedimiento
I-579		1-(3-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-fenil-etanona		(400 MHz, DMSO-D_6) d ppm 1.76 (d, J = 6.57 Hz, 3H) 2.54 - 2.55 (m, 3H) 5.90 - 5.94 (m, 2H) 6.10 (q, J = 6.57 Hz, 1H) 6.93 (d, J = 1.77 Hz, 1H) 7.39 (t, J = 8.59 Hz, 1H) 7.46 (t, J = 7.83 Hz, 1H) 7.51 (dd, J = 9.09, 5.05 Hz, 1H) 7.63 (d, J = 8.34 Hz, 1H) 7.76 (d, J = 7.83 Hz, 1H) 7.81 – 7.83 (m, 1H) 7.85 (d, J = 2.02 Hz, 1H)	419	19
I-580		3-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-5-(3,5-difluoro-fenil)-piridin-2-ilamina		(400 MHz, DMSO-D_6) d ppm 1.82 (d, J = 6.57 Hz, 3H) 6.06 - 6.10 (m, 2H) 6.18 (q, J = 6.57 Hz, 1H) 7.01 (d, J= 1.77 Hz, 1H) 7.06 - 7.19 (m, 3H) 7.45 (t, J = 8.84 Hz, 1H) 7.58 (dd, J = 9.09, 5.05 Hz, 1H) 7.95 (d, J = 2.02 Hz, 1H)	413	19
I-581		3-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-5-(2,5-dicloro-fenil)-piridin-2-ilamina		(400 MHz, DMSO-D_6) d ppm 1.90 (d, J= 6.82 Hz, 3H) 6.10 (q, J = 6.57 Hz, 1H) 6.17 - 6.19 (m, 2H) 6.84 (d, J = 1.77 Hz, 1H) 7.44 - 7.51 (m, 2H) 7.56 (t, J = 8.59 Hz, 1H) 7.59 - 7.70 (m, 3H)	446	19
I-582		(4-{6-amino-5-[1-(2,6-dicloro-4-trifluorometil-fenil)-etoxi]-piridin-3-il}-fenil)-((3R, 5S)-3,5-dimetil-piperazin-1-il)-metanona		Pasado CHN 1.0 eq AcOH	567	18/20
I-583		3-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-5-(3-etoxi-fenil)-piridin-2-ilamina		(400 MHz, DMSO-D_6) d ppm 1.33 (t, J = 6.82 Hz, 3H) 1.82 (d, J = 6.57 Hz, 3H) 3.99 - 4.09 (m, 2H) 5.88 - 5.91 (m, 2H) 6.13 (q, J = 6.57 Hz, 1H) 6.80 (dd, J = 8.08, 2.27 Hz, 1H) 6.84 (t, J = 2.02 Hz, 1H) 6.92 (d, J = 1.77 Hz, 1H) 6.96 (d, J = 7.58 Hz, 1H) 7.26 (t, J = 7.83 Hz, 1H) 7.46 (t, J = 8.59 Hz, 1H) 7.57 (dd, J = 8.84, 5.05 Hz, 1H) 7.83 (d, J = 1.77 Hz, 1H)	421	19
I-584		5-(3-cloro-fenil)-3-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-2-ilamina		(400 MHz, DMSO-D_6) d ppm 1.87 (d, J = 6.57 Hz, 3H) 6.03 - 6.06 (m,2H) 6.16 – 6.24 (m, 1H) 7.02 (d, J = 2.02 Hz, 1H) 7.35 (td, J = 6.82, 1.77 Hz, 1H) 7.41 - 7.53 (m, 4H) 7.62 (dd, J = 8.84, 5.05 Hz, 1H) 7.93 (d, J = 2.02Hz, 1H)	411	19
I-585		3-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-5-(4-fluoro-3-metil-fenil)-piridin-2-ilamina		(400 MHz, DMSO-D_6) d ppm 1.58 (d, J = 6.57 Hz, 3H) 2.01 - 2.02 (m, 3H) 5.62- 5.64 (m, 2H) 5.89 (q, J = 6.82 Hz, 1H) 6.68 (d, J = 1.77 Hz, 1H) 6.90 (t, J = 8.84 Hz, 1H) 6.96 - 7.04 (m, 2H) 7.22 (t, J = 8.59 Hz, 1H) 7.34 (dd, J = 9.09, 5.05 Hz, 1 H) 7.56 (d, J = 1.77 Hz, 1H)	409	19
I-586		3-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-5-(3-trifluorometil-fenil)-piridin-2-ilamina		(400 MHz, DMSO-D_6) d ppm 1.84 (d, J = 6.57 Hz, 3H) 6.05 - 6.07 (m, 2H) 6.14 - 6.21 (m, 1H) 6.99 (d, J = 1.77 Hz, 1H) 7.46 (t, J = 8.59 Hz, 1H) 7.56 (dd, J = 8.84, 5.05 Hz, 1H) 7.59 - 7.65 (m, 3H) 7.76 - 7.80 (m, 1H) 7.95 (d, J = 1.77 Hz, 1H)	445	19

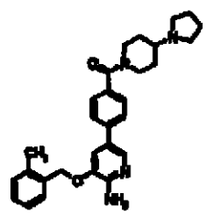
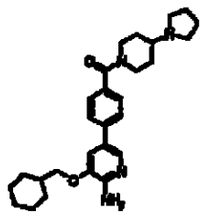
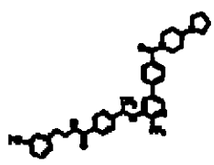
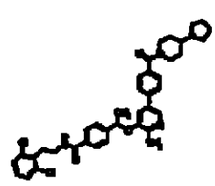
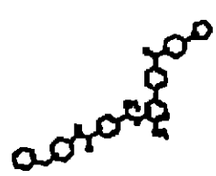
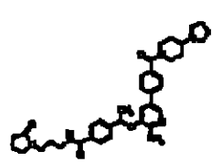
No.	Estructura	Nombre	Ki (μM) o I (%)	^{1}H- NMR	Ms m/z (M+H)	Procedimiento
I-587		3-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-5-(3-fluoro-fenil)-piridin-2-ilamina		(400 MHz, DMSO-D_6) d ppm 1.82 (d, J = 6.57 Hz, 3H) 5.98 - 6.00 (m, 2H) 6.13 - 6.20 (m, 1H) 6.99 (d, J = 1.77 Hz, 1H) 7.05 - 7.11 (m, 1H) 7.21 - 7.27 (m, 2H) 7.39 - 7.49 (m, 2H) 7.59 (dd, J = 9.09, 5.05 Hz, 1H) 7.90 (d, J = 2.02 Hz, 1H)	395	19
I-588		3-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-5-(3-trifluorometoxi-fenil)-piridin-2-ilamina		(400 MHz, DMSO-D_6) d ppm 1.60 (d, J = 6.57 Hz, 3H) 5.80 – 5.84 (m, 2 H) 5.90 - 5.98 (m, 1H) 6.73 (d, J = 2.02 Hz, 1H) 7.00 - 7.07 (m, 2H) 7.20 - 7.30 (m, 3H) 7.34 (dd, J = 8.84, 4.80 Hz, 1H) 7.68 (d, J = 1.77 Hz, 1H)	461	19
I-589		5-benzo[1,3]dioxol-5-il-3-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]- -piridin-2-ilamina		(400 MHz, DMSO-D_6) d ppm 1.82 (d, J = 6.57 Hz, 3H) 5.81 - 5.83 (m, 2H) 8.03 - 6.04 (m, 2H) 6.10 - 6.17 (m, 1H) 6.83 - 6.96 (m, 4H) 7.48 (t, J = 8.84 Hz, 1H) 7.58 (dd, J = 9.09, 5.05 Hz, 1H) 7.76 (d, J = 2.02 Hz, 1H)	421	19
I-590		3-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-fenol		(400 MHz, DMSO-D_6) d ppm 1.95 (d, J = 6.82 Hz, 3H) 5.98 - 6.00 (m, 2H) 6.22- 6.28 (m, 1H) 6.78 – 6.81 (m, 1H) 6.89 - 6.93 (m, 2H) 7.04 (d, J = 1.77 Hz, 1H) 7.29 (t, J = 8.08 Hz, 1H) 7.58 (t, J = 9.09, 8.59 Hz, 1H) 7.71 (dd, J = 8.84, 4.80 Hz, 1H 7.89 (d, J = 1.77 Hz, 1H) 9.55 - 9.57 (m, 1H)	393	19
I-591		(3-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-fenil)-metanol		(400 MHz, DMSO-D_6) d ppm 1.83 (d, J = 6.57 Hz, 3H) 4.52 (d, J = 5.31 Hz, 2H) 5.16 - 5.22 (m, 1H) 5.68 - 5.90 (m, 2H) 6.11 - 6.17 (m, 1H) 6.96 (d, J = 1.52 Hz, 1H) 7.20 - 7.28 (m, 2H) 7.31 - 7.36 (m, 2H) 7.46 (t, J = 8.84 Hz, 1H) 7.58 (dd, J = 9.0.9, 5.05 Hz, 1H) 7.83 (d, J = 1.77 Hz, 1H)	407	19
I-592		3-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-benzonitrilo		(400 MHz, DMSO-D_6) d ppm 1.88 (d, J = 6.57 Hz, 3H) 6.10 - 6.12 (m, 2H) 6.24 (q, J = 6.57 Hz, 1H) 7.12 (d, J = 1.77 Hz, 1H) 7.51 (t, J = 8.59 Hz, 1H) 7.60 - 7.68 (m, 2H) 7.77 (d, J = 7.83 Hz, 1H) 7.81 (d, J = 8.08 Hz, 1H) 7.94 - 7.96 (m, 1H) 8.00 (d, J = 1.77 Hz, 1H)	402	19
I-593		3-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-5-(3-metoxi-fenil)-piridin-2-ilamina		(400 MHz, DMSO-D_6) d ppm 1.83 (d, J = 6.57 Hz, 3H) 3.79 - 3.80 (m, 3H) 5.91 - 5.92 (m, 2H) 6.11 - 6.16 (m, 1H) 6.81 - 6.84 (m, 1H) 6.86 - 6.89 (m, 1H) 6.93 (d, J = 1.52 Hz, 1H) 6.97 - 7.01 (m, 1H) 7.29 (t, J = 8.34, 7.83 Hz, 1H) 7.46 (t, J 8.84 Hz, 1H) 7.59 (dd, J = 9.09, 5.05 Hz, 1H) 7.85 (d, J = 1.77 Hz, 1H)	407	19
I-594		3-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-5-(3,5 dicloro-fenil)-piridin-2-ilamina		(400 MHz, DMSO-D_6) d ppm 1.83 (d, J = 6.57 Hz, 3H) 6.10 - 6.12 (m, 2H) 6.16 - 6.22 (m, 1H) 7.00 (d, J = 1.77 Hz, 1H) 7.44 - 7.49 (m, 4H) 7.58 (dd, J = 9.09, 5.31 Hz, 1H) 7.95 (d, J = 2.02 Hz, 1H)	446	19

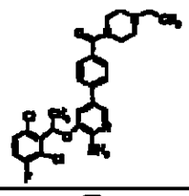
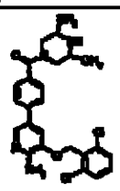
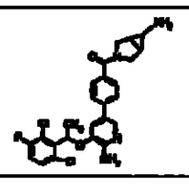
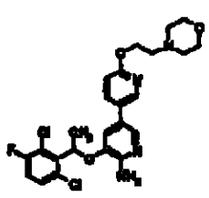
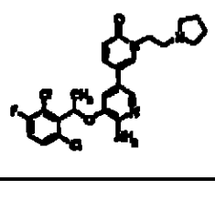
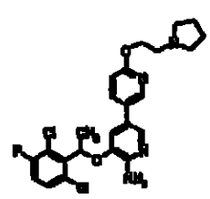
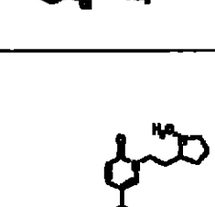
No.	Estructura	Nombre	Ki (μM) o I (%)	^{1}H- NMR	Ms m/z (M+H)	Procedimiento
I-595		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,5- dimetil- fenil)- piridin- 2- ilamina		(400 MHz, DMSO- D_6) d ppm 1.80 (d, J = 6.82 Hz, 3H) 1.90 - 1.93 (m, 3H) 2.24 - 2.27 (m, 3H) 5.81 - 5.83 (m, 2H) 6.00 (q, J = 6.82, 6.32 Hz, 1H) 6.57 (d, J = 1.77 Hz, 1H) 6.79 - 6.82 (m, 1H) 6.98 - 7.03 (m, 1H) 7.10 (d, J = 7.83 Hz, 1H) 7.45 - 7.52 (m, 2H) 7.58 (dd, J = 8.84, 5.05 Hz, 1H)	405	19
I-596		5- (5- cloro- 2- metoxi- fenil)- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina		(400 MHz, DMSO- D_6) d ppm 1.79 (d, J = 6.57 Hz, 3H) 3.61 - 3.63 (m, 3H) 5.89 - 5.91 (m, 2H) 5.97 - 6.03 (m, 1H) 6.86 (d, J = 1.77 Hz 1H) 7.06 (d, J = 8.84 Hz, 1H) 7.15 (d, J = 2.78 Hz, 1H) 7.29 (dd, J = 8.84, 2.53 Hz, 1H) 7.49 (t, J = 8.59 Hz, 1H) 7.59 (dd, J = 9.09, 5.31 Hz, 1H) 7.63 (d, J = 1.77 Hz, 1H)	441	19
I-597		5- (3- cloro- 4- fluoro- fenil)- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina		(400 MHz, DMSO- D_6) d ppm 1.83 (d, J = 6.57 Hz, 3H) 5.98 - 6.00 (m, 2H) 6.14 - 6.20 (m, 1H) 6.98 (d, J = 1.77 Hz, 1H) 7.42 - 7.45 (m, 2H) 7.47 (d, J = 8.59 Hz, 1H) 7.55 - 7.60 (m, 2H) 7.87 (d, J = 2.02 Hz, 1H)	429	19
I-598		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (5- fluoro- 2- metoxi- fenil)- piridin- 2- ilamina		(400 MHz, DMSO- D_6) d ppm 1.79 (d, J = 6.57 Hz, 3H) 3.59 - 3.60 (m, 3H) 5.88 - 5.91 (m, 2H) 6.00 (q, J = 6.82 Hz, 1H) 6.90 (d, J = 1.77 Hz, 1H) 6.99 - 7.10 (m, 3H) 7.48 (t, J = 8.84 Hz, 1H) 7.59 (dd, J = 9.09, 5.31 Hz, 1H) 7.64 (d, J = 2.02 Hz, 1H)	425	19
I-599		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3- isopropil- fenil)- piridin- 2- ilamina		(400 MHz, DMSO- D_6) d ppm 1.20 - 1.25 (m, 6H) 1.83 (d, J = 6.57 Hz, 3H) 2.86 – 2.94 (m, 1H) 5.88 - 5.91 (m, 2H) 6.13 (q, J = 6.32 Hz, 1H) 6.89 (d, J = 1.77 Hz, 1H) 7.11 - 7.15 (m, 2H) 7.23 - 7.31 (m, 2H) 7.47 (t, J = 8.59 Hz, 1H) 7.58 (dd, J = 8.84, 4.80 Hz, 1H) 7.83 (d, J = 2.02 Hz, 1H)	419	19
I-600		5- (3- cloro- 4- trifluorometil- fenil)- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina		(400 MHz, DMSO- D_6) d ppm 1.83 (d, J = 6,57 Hz, 3H) 6.11 - 6.13 (m, 2H) 6.17 (q, J = 6.57 Hz, 1H) 6.99 (d, J = 1.77 Hz, 1H) 7.46 (t, J = 8.84 Hz, 1H) 7.56 (dd, J = 9.09, 5.05 Hz, 1H) 7.68 (d, J = 1.77 Hz, 1H) 7.72 (d, J = 8.59 Hz, 1H) 7.80 (dd, J = 8.34, 1.77 Hz, 1H) 7.95 (d, J = 2.02 Hz, 1H)	478.90	19
I-601		4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- piridin- 2- il}- benzonitrilo		(400 MHz, DMSO- D_6) d ppm 1.83 (d, J = 6.57 Hz, 3H) 6.13 - 6.22 (m, 3H) 7.06 (d, J = 177 Hz, 1H) 7.45 (t, J = 8.59 Hz, 1H) 7.57 (dd, J = 9.09, 5.05 Hz, 1H) 7.63 (d, J = 8.59 Hz, 2H) 7.84 (d, J = 8.59 Hz, 2H) 7.97 (d, J = 1.77 Hz, 1H)	402	19
I-602		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3,4- difluoro- fenil)- piridin- 2- ilamina		(400 MHz, DMSO- D_6) d ppm 1.82 (d, J = 6.82 Hz, 3H) 5.96 - 6.00 (m, 2H) 6.17 (q, J = 6.57 Hz, 1H) 6.99 (d, J = 1.77 Hz, 1H) 7.22- 7.27 (m, 1H) 7.41 – 7.52 (m, 3H) 7.58 (dd, J = 9.09, 5.05 Hz, 1H) 7.87 (d, J = 2. 02 Hz, 1H)	413	19

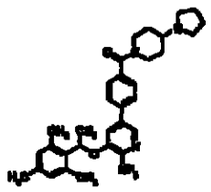
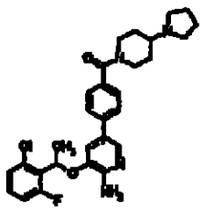
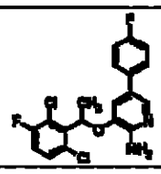
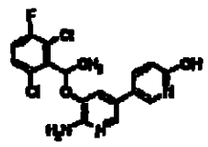
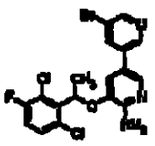
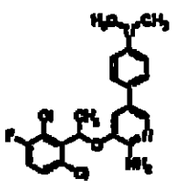
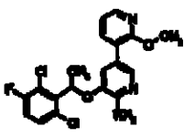
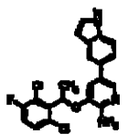
No.	Estructura	Nombre	Ki (μM) o I (%)	^{1}H- NMR	Ms m/z (M+H)	Procedimiento
I-603		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil[1,4]diacefan- 1- il)- metanona	0.0095	(400 MHz, DMSO- D_6) d ppm 1.73 (m, 1H) 1.80 (d, J = 6.82 Hz, 3H) 1.84 (m, 1H) 2.26 (d, J = 21.98 Hz, 2H) 2.53 (m, 2H) 2.63 (m, 2H) 3.40 (m, 2H) 3.60 (m, 2H) 5.95 (s, 2H) 6.14 (d, J = 6.57 Hz, 1H) 6.99 (s, 1H) 7.36 (d, J = 7.58 Hz, 2H) 7.44 (m, 3H) 7.57 (dd, J = 8.97, 4.93 Hz, 1H) 7.86 (d, J = 1.77 Hz, 1H)	517	20
I-604		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- [1,4]diacefan- 1- il- metanona	0.031	(400 MHz, DMSO- D_6) d ppm 1.81 (t, J = 6.19 Hz, 3H) 1.90 (m, 2H) 2.96 (m, 2H) 3.10 (d, J = 36.88 Hz, 2H) 3.45 (m, 2H) 3.7 (m, 2H) 5.96 (s, 2H) 6.14 (q, J = 6.82 Hz, 1H) 6.99 (d, J = 1.52 Hz, 1H) 7.44 (m, 5H) 7.56 (dd, J = 8.97, 4.93 Hz, 1H) 7.87 (d, J = 1.77 Hz, 1H)	503	20/21
I-605		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- piperazin- 1- il- metanona	0.0475	(400 MHz, DMSO- D_6) d ppm 1.80 (d, J = 6.57 Hz, 3H) 2.72 (m, 4H) 3.36 (m, 2H) 3.52 (m, 2H) 5.96 (s, 2H) 6.14 (q, J = 6.74 Hz, 1H) 6.99 (d, J = 1.77 Hz, 1H) 7.37 (m, 2H) 7.44 (m, 3H) 7.57 (dd, J = 8.97, 4.93 Hz, 1H) 7.87 (d, J = 1.77 Hz, 1H)	489	20/21
I-606		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- vinil- piridin- 2- ilamina	0.655	(400 MHz, CLOROFORMO- D) d, ppm 1.83 (d, J = 6.57 Hz, 3H) 4.84 (s, 2H) 5.03 (d, J = 11.12 Hz, 1H) 5.38 (d, J = 17.43 Hz, 1H) 6.06 (q, J = 6.82 Hz, 1H) 6.49 (dd, J = 17.68, 10.86 Hz, 1H) 6.90 (d, J = 1.77 Hz, 1H) 7.04 (dd, J = 8.84, 7.83Hz, 1H) 7.29 (dd, J = 8.84, 4.80 Hz, 1H) 7.55 (d, J = 1.77 Hz, 1H)	327	19
I-607		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R- 4S)- 3,4- dihidroxi- pirrolidin- 1- il)- metanona	0.058	(400 MHz, DMSO- D_6) d ppm 1.81 (d, J = 6.82 Hz, 3H) 3.28 (m, 2H) 3.54 (m, 2H) 3.97 (d, J = 4.04 Hz, 2H) 4.08 (d, J = 4.29 Hz, 2H) 5.10 (br, 2H) 5.98 (d, 2H) 7.00 (d, J = 1.77 Hz, 1H) 7.45 (m, 3H) 7.48 (m, 2H) 7.57 (dd, J = 8.97, 4.93 Hz, 1H) 7.88 (d, J = 1.77 Hz, 1H)	506	20/21
I-608		5- [(1- benzil- pirrolidin- 3- ilamina)- metil]- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina	0%	(400 MHz, DMSO- D_6) d ppm 1.34 (m, 1H) 1.74 (d, J = 5.94 Hz, 3H) 1.78 (m, 1H) 2.08 (m, 1H) 2.40 (m, 2H) 2.54 (m, 1H) 2.89 (m, 1H) 3.33 (s, 2H) 3.49 (s, 2H) 5.52 (s, 2H) 5.94 (q, J = 6.57 Hz, 1H) 6.68 (s, 1H) 7.27 (m, 5H) 7.36 (m, 1H) 7.39 (m, 1H) 7.48 (m, 1H)	489	23
I-609		4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- acetidin- 3- il- benzamida	0.045	(400 MHz, DMSO- D_6) d ppm 1.80 (d, J = 6.57 Hz, 3H) 2.87 (m, 1H) 3.43 (m, 1H) 3.81 (m, 2H) 4.74 (m, 1H) 6.00 (s, 2H) 6.13 (q, J = 6.48 Hz, 1H) 6.96 (dd, J = 6.57, 1.77 Hz, 1H) 7.45 (m, 3H) 7.54 (dd, J = 8.97, 4.93 Hz, 1H) 7.87 (m, 3H)	475	20/21
I-610		4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- N- dimetil- bencenosulfonamida	0.069	(400 MHz, CLOROFORMO- D) d ppm 1.87 (d, J = 6.82 Hz, 3H) 2.72 (s, 6H) 4.99 (s, 2H) 6.12 (q, J = 6.57 Hz, 1H) 6.99 (d, J = 1.77 Hz, 1H) 7.07 (m, 1H) 7.32 (dd, J = 8.84, 4.80 Hz, 1H) 7.50 (m, 2H) 7.76 (d, J = 8.59 Hz, 2H) 7.91 (d, J = 1.77 Hz, 1H)	484	29

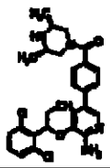
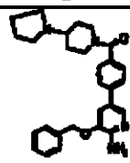
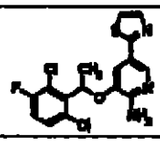
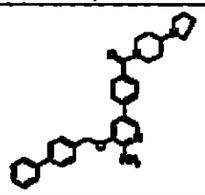
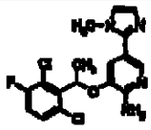
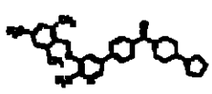
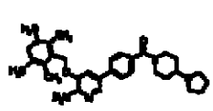
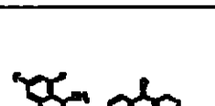
No.	Estructura	Nombre	Ki (μM) o I (%)	^{1}H- NMR	Ms m/z (M+H)	Procedimiento
I-611		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (6- metoxi- 1H- benzoimidazol- 2- il)- piridin- 2- ilamina		(400 MHz, MeOD) d ppm 1.72 (d, J = 6.57 Hz, 3H) 3.69 (s, 3H) 4.78 (s, 2H) 6.13 (q, J = 6.57 Hz, 1H) 6.71 (dd, J = 8.84, 2.27 Hz, 1H) 6.88 (d, J = 2.02 Hz, 1H) 7.04 (m, 1H) 7.26 (m, 2H) 7.40 (d, J = 1.77 Hz, 1H) 8.03 (d, J = 2.02 Hz 1H)	447	24
I-612		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (6- metoxi- 1- metil- 1H- benzoimidazol- 2- il)- piridin- 2- ilamina		(400 MHz, MeOD) d ppm 1.78 (d, J = 6.57 Hz, 3H) 3.51 (s, 3H) 3.75 (s, 3H) 6.10 (q, J = 6.32 Hz, 1H) 6.90 (m, 1H) 6.92 (m, 1H) 7.13 (m, 1H) 7.35 (m, 2H) 7.80 (d, J = 7.33 Hz, 1H)	461	24
I-613		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [4- (4- metil- [1,4]diazepano- 1- sulfonil)- fenil]- piridin- 2- ilamina		(400 MHz, MeOD) d ppm 1.83 (m, 2H) 1.87 (d, J = 6.57 Hz, 3H) 2.66 (m, 4H) 3.35 (m, 2H) 3.40 (m, 2H) 6.20 (q, J = 6.65 Hz, 1H) 7.02 (d, J = 1.77 Hz, 1H) 7.20 (t, J = 8.59 Hz, 1H) 7.43 (dd, J = 8.97, 4.93 Hz, 1H) 7.54 (d, J = 8.34 Hz, 2H) 7.77 (d, J = 8.59 Hz, 2H) 7.81 (d, J = 1.26 Hz, 1H)	553	29
I-614		Amida del ácido carboxílico 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (1- metil- 1H- pirazol- 4- il)- piridin- 2- ilamina		(400 MHz, DMSO- D_6) d ppm 1.82 (d, J = 6.57 Hz, 3H) 3.92 (s, 3H) 5.96 (s, 2H) 6.17 (q, J = 6.48 Hz, 1H) 7.03 (d, J = 1.77 Hz, 1H) 7.35 (dd, J = 8.59, 1.26 Hz, 1H) 7.44 (t, J = 8.72 Hz, 1H) 7.56 (m, 2H) 7.91 (d, J = 2.02 Hz, 1H) 8.03 (d, J = 8.59 Hz, 1H)	475	26
I-615		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (1- metil- 1H- pirazol- 4- il)- piridin- 2- ilamina		(400 MHz, CLOROFORMO- D) D ppm 1.84 (d, J = 6.82 Hz, 3H) 3.89 (s, 3H) 4.76 (s, 2H) 6.05 (q, J = 6.57 Hz, 1H) 6.84 (d, J = 1.77 Hz, 1H) 7.03 (m, 1H) 7.28 (dd, J = 8.97, 4.93 Hz, 1H) 7.40 (s, 1H) 7.53 (s, 1H) 7.74 (d, J = 1.77 Hz, 1H)	381	19*
I-616		(4- {6- amino- 5- [1- (2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- (3,5- dimetil- piperazin- 1- il)- metanona	3%	(400 MHz, DMSO- D_6) d ppm 9.29 (d, J = 9.60 Hz, 1H) 8.63 (d, J = 10.86 Hz, 1H) 7.84 - 7.94 (m, 2H) 7.72 (t, J = 7.96 Hz, 3H) 7.47 - 7.57 (m, 6H) 7.35 (s, 1H) 5.97 - 6.05 (m, 1H) 3.37 (s, 2H) 1.69 (d, J = 6.06 Hz, 3H) 1.15 (s, 5 H) 1.06 (s, 1H)	500	33
I-617		(4- {6- amino- 5- [1- (3- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- (3,5- dimetil- piperazin- 1- il)- metanona	2%	(400 MHz, DMSO- D_6) d ppm 9.26 (s, 2H) 8.64 (s, 2H) 7.93 (s, 2H) 7.84 (d, J = 1.52 Hz, 2H) 7.81 (d, J = 7.58 Hz, 2H) 7.66 (s, 2H) 7.60 (d, J = 8.34 Hz, 5H) 7.53 - 7.59 (m, 2H) 7.46 (d, J = 8.34 Hz, 4H) 6.01 (q, J = 6.32 Hz, 2H) 3.32 (s, 4H) 3.03 (s, 1H) 2.75 (s, 1H) 1.61 (d, J = 6.32 Hz, 5H) 1.13 (s, 7H)	500	32
I-618		7- [4- (3,5- dimetil- piperazine- 1- carbonil)- fenil]- 2- fenil- 4H- pirido[3,2][1,4]oxazin- 3- ona	0%	(400 MHz, DMSO- D_6) d ppm 8.53 (s, 2H) 8.33 (d, J = 2.02 Hz, 2H) 7.84 (d, J = 4.02 Hz, 2H) 7.80 (d, J = 8.34 Hz, 5H) 7.36 - 7.42 (m, 12H) 5.93 (s, 2H) 4.55 (s,1H) 3.73 (s, 3H) 3.40 (s, 6H) 1.19 (s, 10H)	444	32

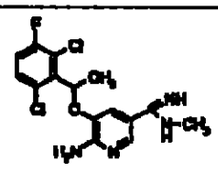
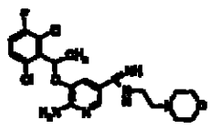
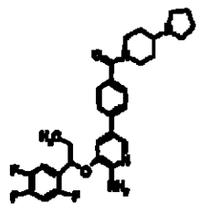
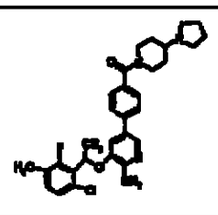
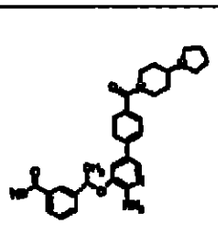
No.	Estructura	Nombre	Ki (μM) o I (%)	^{1}H- NMR	Ms m/z (M+H)	Procedimiento
I-619		{4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona	16%	(400 MHz, DMSO- D_6) d ppm 7.97 (d, J = 1.77 Hz, 1H) 7.79 (s, 1H) 7.66 - 7.74 (m, 3H) 7.48 (d, J = 1.77 Hz, 2H) 7.41 (d, J = 8.34 Hz, 2H) 7.24 (s, 1H) 5.91 (s, 1H) 5.40 (s, 2H) 3.61 (s, 1H) 2.61 - 2.70 (m, 3H) 2.33 (s, 1H) 2.17 (s, 1H) 1.95 - 2.06 (m, 1H) 1.47 (s, 1H) 1.23 (s, 7H) 1.00 (s, 3H) 0.80 - 0.92 (m, 6H)	504	32
I-620		{4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona	5%	(400 MHz, DMSO- D_6) d ppm 8.02 (s, 1H) 7.96 (s, 1H) 7.85 (d, J = 8.34 Hz, 2H) 7.51 - 7.62 (m, 3H) 7.23 (t, J = 8.08 Hz, 2H) 5.43 (s, 2H) 4.09 (s, 1H) 3.37 (s, 1H) 1.40 (s, 9H) 1.14 (d, J = 2.27 Hz, 3H) 1.08 (d, J = 16.42 Hz, 3H)	454	34
I-621		[4- (6- amino- 5- benciloxi- piridin- 3- il)- fenil]- (3,5- dimetil- piperazin- 1- il)- metanona	6%	(400 MHz, DMSO- D_6) d ppm 9.35 (s, 1H) 8.70 (s, 1H) 7.96 (s, 2H) 7.78 (d, J = 8.59 Hz, 4H) 7.55 (d, J = 8.08 Hz, 5H) 7.42 (t, J = 7.20 Hz, 2H) 7.35 (t, J = 7.33 Hz, 1H) 5.40 (s, 2H) 3.39 (s, 2H) 3.16 (s, 1H) 1.20 (s, 4H)	418	3
I-622		(4- [6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- etil- piperazin- 1- il)- metanona	0.375	(400 MHz, DMSO- D_6) d ppm 7.95 (d, J = 1.77 Hz, 1H) 7.57 (d, J = 8.34 Hz, 2H) 7.52 (s, 1H) 7.45 (d, J = 8.08 Hz, 3H) 7.25 (d, J = 1.77 Hz, 1H) 6.11 (s, 1H) 5.95 (s, 2H) 3.62 (s, 1H) 3.49 (s, 1H) 2.44 (s, 2H) 2.41 (d, J = 7.07 Hz, 4H) 1.85 (d, J = 6.32 Hz, 3H) 1.06 (t, J = 7.20 Hz, 3H)	502	4
I-623		[4- (6- amino- 5- benciloxi- piridin- 3- il)- fenil]- (4- etil- piperazin- 1- il)- metanona	7%	(400 MHz, DMSO- D_6) d ppm 7.91 (d, J = 2.02 Hz, 1H) 7.65 (d, J = 8.34 Hz, 2H) 7.53 (d, J = 7.33 Hz, 2H) 7.44 (d, J = 1.77 Hz, 1H) 7.37 - 7.42 (m, 3H) 7.32 (t, J = 7.33 Hz, 1H) 5.94 (s, 2H) 5.25 (s, 2H) 3.60 (s, 1H) 3.38 (s, 1H) 2.30 - 2.41 (m, 5H) 0.99 (t, J = 7.20 Hz, 3H)	418	34
I-624		{4- [6- amino- 5- (2- metil- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona	0%	(400 MHz, DMSO- D_6) d ppm 9.40 (s, 1H) 8.77 (s, 1H) 7.98 (d, J = 1.52 Hz, 1H) 7.77 - 7.88 (m, 4H) 7.57 (d, J = 8.34 Hz, 2H) 7.53 (d, J = 7.33 Hz, 1H) 7.21 - 7.31 (m, 3H) 5.37 (s, 2H) 3.39 (s, 2H) 2.37 (s, 3H) 1.20 (s, 4H)	432	34
I-625		Metil ester del acido 3- {2- amino- 5- [4- (4- pirrolidin- 1- il- piperidina- 1- carbonil)- fenil]- piridin- 3- iloximetil}- benzoico	6%	(400 MHz, DMSO- D_6) d ppm 9.78 (s, 1H) 8.12 (s, 1H) 7.92 - 7.98 (m, 2H) 7.88 (d, J = 7.58 Hz, 1H) 7.74 - 7.83 (m, 3H) 7.59 (t, J = 7.71 Hz, 2H) 7.46 (d, J = 8.34 Hz, 2H) 5.47 (s, 2H) 3.86 s, 3H) 3.50 (s, 2H) 3.41 (s, 1H) 3.10 (s, 2H) 2.00 (s, 3H) 1.85 (s, 2H) 1.53 (s, 2H)	516	6
I-626		Metil ester del acido 3- {2- amino- 5- [4- (3,5- dimetil- piperazina- 1- carbonil)- fenil]- piridin- 3- iloximetil}- benzoico	0%	(400 MHz, DMSO- D_6) d ppm 9.31 (s, 2H) 8.67 (s, 2H) 8.12 (s, 2H) 7.92 - 7.99 (m, 4H) 7.88 (d, J = 7.83 Hz, 2H) 7.75 - 7.84 (m, 6H) 7.53 - 7.63 (m, 6H) 5.48 (s, 4H) 3.81 - 3.91 (m, 6H) 3.39 (s, 4 H) 3.13(s, 1H) 1.20 (s,7H)	476	34

No.	Estructura	Nombre	Ki (μM) o I (%)	^{1}H- NMR	Ms m/z (M+H)	Procedimiento
I-627		[4- [6- amino- 5- (2- metil- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	6%	(400 MHz, DMSO- D_6) d ppm 9.91 (s, 1H) 7.95 (d, J = 1.52 Hz, 1H) 7.85 (s, 1H) 7.80 (d, J = 8.34 Hz, 2H) 7.53 (d, J = 7.07 Hz, 1H) 7.49 (d, J = 8.34 Hz, 2H) 7.21 - 7.31 (m, 3H) 5.36 (s, 2H) 4.56 (s, 1H) 3.68 (s, 1H) 3.51 (s, 2H) 3.41 (s, 1H) 3.10 (s, 3H) 2.82 (s, 1H) 2.37 (s, 3H) 1.99 (s, 3H) 1.79 - 1.90 (m, 2H) 1.56 (s, 2H)	472	6
I-628		[4- (6- amino- 5- ciclohexilmetoxi- piridin- 3- il)- fenil]- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	7%	(400 MHz, DMSO- D_6) d ppm 7.90 (d, J = 1.52 Hz, 1H) 7.79 (d, J = 8.34 Hz, 3H) 7.66 (s, 1H) 7.44 - 7.55 (m, 2H) 4.03 (d, J = 6.06 Hz, 2H) 3.83 (s, 1H) 3.67 (s, 1H) 3.51 (s, 2H) 3.39 (s, 1H) 3.09 (s, 2H) 2.82 (s, 1H) 2.14 (s, 2H) 1.99 (s, 3H) 1.79 - 1.91 (m, 5H) 1.64 - 1.76 (m, 3H) 1.54 (s, 2H) 1.20 - 1.30 (m, 2H) 1.07 (d, J = 11.62 Hz, 2H)	464	6
I-629		4- (1- [2- amino- 5- [4- (4- pirrolidin- 1- il- piperidina- 1- carbonil)- fenil]- piridin- 3- iloxi- etil)- [2- (3- hidroxi- fenil)- etil]- benzamida	7%	(400 MHz, DMSO- D_6) d ppm 9.76 (s, 1H) 8.51 (t, J = 5.56 Hz, 1H) 7.86 (d, J = 1.52 Hz, 2H) 7.79 (d, J = 8.34 Hz, 2H) 7.63 (dd, J = 14.40, 8.34 Hz, 5H) 7.45 (d, J = 8.34 Hz, 2H) 7.04 (t, J = 7.96 Hz, 1H) 6.55 - 6.65 (m, 3H) 6.00 (d, J = 6.32 Hz, 1H) 3.49 (s, 2H) 3.34 - 3.45 (m, 3H) 3.09 (s, 3H) 2.75 (s, 1H) 2.65- 2.74 (m, 2H) 2.13 (s, 1H) 1.99 (s, 3H) 1.78 – 1.89 (m, 2H) 1.65 (d, J = 6.32 Hz, 3H) 1.52 (s, 2H)	635	6
I-630		4- (1- [2- amino- 5- [4- (4- pirrolidin- 1- il- piperidina- 1- carbonil)- fenil]- piridin- 3- iloxi- etil)- [2- (2,6- dicloro- fenil)- etil]- benzamida	3%	(400 MHz, DMSO- D_6) d ppm 9.80 (s, 1H) 8.62 (t, J = 5.81 Hz, 1H) 7.85 (d, J = 1.26 Hz, 1H) 7.78 (d, J = 8.34 Hz, 3H) 7.62 (d,d, J = 12.63, 8.34 Hz, 5H) 7.39 - 7.49 (m, 4H) 7.21 - 7.30 (m, 1H) 5.98 (d, J = 6.32 Hz, 1H) 3.65 (s, 1H) 3.40 - 3.51 (m, J = 6.63, 6.63, 6.63, 6.63 Hz, 4H) 3.03 - 3.15 (m, 5H) 2.82 (s, 1H) 2.13 (s, 1H) 1.98 (s, 3H) 1.78 – 1.89 (m, 2H) 1.65 (d, J = 6.08 Hz, 3H) 1.53 (s, 2H)	688	6
I-631		4- (1- [2- amino- 5- [4- (4- pirrolidin- 1- il- piperidina- 1- carbonil)- fenil]- piridin- 3- iloxi- etil)- (1- benzil- piperidin- 4- il)- benzamida	3%	(400 MHz, DMSO- D_6) d ppm 7.75 - 7.82 (m, 2H) 7.56 - 7.67 (m, 4H) 7.39 – 7.49 (m, 6H) 4.27 (d, J = 4.80 Hz, 2H) 3.92 (s, 1H) 3.49 (s, 2H) 3.37 (s, 2H) 3.07 (s, 3H) 2.12 (s, 1H) 1.92 - 2.04 (m, 4 H) 1.79 - 1.91 (m, 2H) 1.71 (d, J = 11.87 Hz, 1H) 1.59 - 1.68 (m, 3H) 1.51 (s, 2H)	688	4
I-632		4- (1- [2- amino- 5- [4- (4- pirrolidin- 1- il- piperidina- 1- carbonil)- fenil]- piridin- 3- iloxi- etil)- [3- (2- oxo- pirrolidin- 1- il)- propil]- benzamida	0%	(400 MHz, DMSO- D_6) d ppm 8.39 (s, 1H) 7.77 - 7.85 (m, 3H) 7.61 (t, J = 8.08 Hz, 6H) 7.43 (d, J = 8.34 Hz, 2H) 5.96 (s, 1H) 3.69 (s, 2H) 3.49 (s, 3H) 3.39 (s, 2H) 3.30 (t, J = 6.95 Hz, 3H) 3.14 - 3.22 (m, 4H) 3.09 (s, 3H) 2.18 (t, J = 8.08 Hz, 2H) 2.00 (s, 3H) 1.86 (ddd, J = 15.28, 7.58, 7.45 Hz, 4H) 1.65 (t, J = 6.06 Hz, 5H) 1.52 (s, 2H)	640	6

No.	Estructura	Nombre	Ki (μM) o I (%)	^{1}H- NMR	Ms m/z (M+H)	Procedimiento
I-633		(4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- etil- piperazin- 1- il)- metanona	0.0472	(400 MHz, DMSO- D_6) d ppm 9.85 (s, 1H) 7.91 (d, J = 1.77 Hz, 1H) 7.58 (dd, J = 8.97, 4.93 Hz, 1H) 7.50 - 7.55 (m, 4H) 7.44 - 7.50 (m, 1H) 7.13 (d, J = 1.52 Hz, 1H) 6.27 (q, J = 6.57 Hz, 1H) 3.48 (s, 2H) 3.15 (q, J = 7.07 Hz, 3H) 3.06 (s, 2H) 1.84 (d, J = 6.57 Hz, 3H) 1.22 (t, J = 7.33 Hz, 3H)	518	6
I-634		{4- [6- amino- 5- [1- (2,6- diclorо- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona	10%	(400 MHz, DMSO- D_6) d ppm 9.20 (s, 2H) 8.66 (s, 2H) 7.91 - 8.00 (m, 5H) 7.85 (d, J = 6.82 Hz, 5H) 7.54 - 7.61 (m, 10H) 7.48 - 7.53 (m, 3H) 5.48 (s, 5H) 4.61 (s, 1H) 1.21 (d, J = 4.55 Hz, 9H) 1.15 (s, 3H)	486	34
I-635		(6- amino- 3- aza- biciclo[3.1.0]hex- 3- il)- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- metanona	0.0554	(400 MHz, DMSO- D_6) d ppm 8.14 (d, J = 3.54 Hz, 3H) 7.87 (s, 1H) 7.58 (dd, J = 8.97, 4.93 Hz, 1H) 7.44 - 7.53 (m, 5H) 7.12 (s, 1H) 6.25 (s, 1H) 3.95 (d, J = 11.87 Hz, 1H) 3.69 (s, 2H) 1.96 (d, J = 13.39 Hz, 2H) 1.84 (d, J = 6.57 Hz, 3H)	502	35
I-636		5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 6'- (2- morfolin- 4- il- etoxi)- 3,3'- bipiridinil- 6- ilamina	0.109	(400 MHz, DMSO- D_6) d ppm 8.20 (d, J = 2.27 Hz, 1H) 7.83 (d, J = 1.77 Hz, 1H) 7.79 (dd, J = 8.59, 2.53 Hz, 1H) 7.61 (dd, J = 8.97, 4.93 Hz, 1H) 7.49 (t, J = 8.84 Hz, 1H) 6.98 (d, J = 1.77 Hz, 1H) 6.88 (d, J = 8.59 Hz, 1H) 6.18 (q, J = 6.82 Hz, 1H) 5.92 (s, 2H) 4.41 (t, J = 5.81 Hz, 2H) 3.61 (m, 4H) 2.72 (t, J = 5.81 Hz, 2H) 2.47 - 2.52 (m, 4H) 1.85 (d, J = 6.57 Hz, 3H)	507	36
I-637		6'- amino- 5'- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 1- (2- pirrolidin- 1- il- etil)- 1H- [3,3']bipiridinil- 6- ona	0.692	(400 MHz, DMSO- D_6) d ppm 7.42 - 7.52 (m, 2H) 7.25 .7.35 (m, 2H) 7.22 (t, J = 8.72 Hz, 1H) 6.64 (d, J = 1.52 Hz, 1H) 6.19 (d, J = 9.35 Hz, 1H) 5.89 (q, J = 6.74 Hz, 1H) 5.58 (s, 2H) 3.72 - 3.84 (m, 2H) 2.42 - 2.53 (m, 2H) 1.57 (d, J = 6.57 Hz, 3H) 1.39 - 1.50 (m, 4H)	491	35
I-638		5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 6'- (2- pirrolidin- 1- il- etoxi)- [3,3']bipiridinil- 6- ilamina	0.094	(400 MHz, DMSO- D_6) d ppm 7.98 (d, J = 2.53 Hz, 1H) 7.62 (d, J = 2.02 Hz, 1H) 7.57 (dd, J = 8.59, 2.53 Hz, 1H) 7.40 (dd, J = 8.97, 4.93 Hz, 1H) 7.27 (t, J = 8.72 Hz, 1H) 6.77 (d, J = 1.77 Hz, 1H) 6.66 (d, J = 8.59 Hz, 1H) 5.97 (q, J = 6.57 Hz, 1H) 5.70 (s, 2H) 4.17 (t, J = 5.81 Hz, 2H) 2.56 - 2.65 (m, 2H) 1.63 (d, J = 6.82 Hz, 3H) 1.46 - 1.54 (m, 4H) 0.97 - 1.09 (m, 1H)	491	35
I-639		6'- amino- 5'- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 1- [2- (1- metil- pirrolidin- 2- il)- etil]- 1H- [3,3']bipiridinil- 6- ona	0.513	(400 MHz, DMSO- D_6) d ppm 7.71 (dd, J = 9.60, 1.77 Hz, 2H) 7.46- 7.56 (m, 2H) 7.42 (t, J = 8.72 Hz, 1H) 6.84 (s, 1H) 6.39 (d, J = 9.35 Hz, 1H) 6.10 (q, J = 6.57 Hz, 1H) 5.79 (s, 2H) 3.98- 4.08 (m, 4H) 3.81 - 3.92 (m, 2H) 2.85 - 2.92 (m, 2H) 2.14- 2.18 (m, 7H) 1.93 - 2.05 (m, 5H) 1.84 - 1.89 (m, 2H) 1.76 - 1.82 (m, 4H) 1.52- 1.63 (m, 6H) 1.26 - 1.38 (m, 2H) 1.08 - 1.18 (m, 6H)	505	3

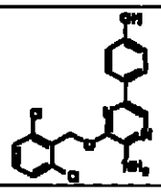
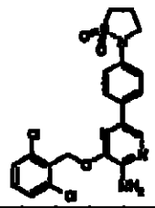
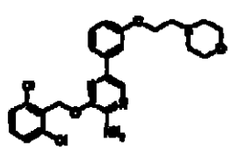
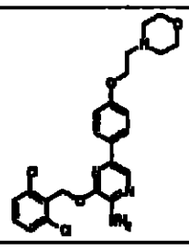
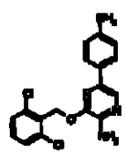
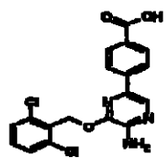
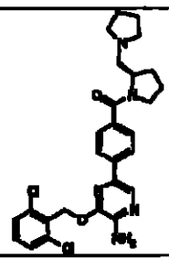
No.	Estructura	Nombre	Ki (μM) o I (%)	^{1}H- NMR	Ms m/z (M+H)	Procedimiento
I-640		(4- {6- amino- 5- [1- (2,4,6- trimetil- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona		(400 MHz, MeOD) d, ppm 7.62 (d, J = 1.52 Hz, 1H) 7.25 - 7.31 (m, 2H) 7.19 - 7.25 (m, 2H) 6.73 (s, 2H) 6.65 (d, J = 1.77 Hz, 1H) 5.65 (q, J = 6.57 Hz, 1H) 4.46 - 4.57 (m, 1H) 3.61 - 3.73 (m, 1H) 2.96 – 3.07 (m, 1H) 2.73 - 2.84 (m, 1H) 2.50 - 2.59 (m, 4H) 2.23 - 2.31 (m, 7H) 2.10 (s, 3H) 1.92 - 2.04 (m, 1H) 1.77 - 1.88 (m, 1H) 1.69 - 1.76 (m, 4H) 1.66 (d, J = 6.82 Hz, 3H) 1.29 - 1.40 (m, 2H)	513	6
I-641		(4- {6- amino- 5- [1- (2- cloro- 6- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona		(400 MHz, MeOD) d, ppm 7.66 (d, J = 2.02 Hz, 1H) 7.28 - 7.39 (m, 4H) 7.12 - 7.23 (m, 2H) 7.07 (d, J = 1.77 Hz, 1H) 6.92 - 7.02 (m, 1H) 5.97 (q, J = 6.06 Hz, 1H) 4.44 - 4.56 (m, 1H) 3.62 - 3.74 (m, 1H) 2.96 - 3.08 (m, 1H) 2.72 - 2.84 (m, 1H) 2.48 - 2.59 (m, 4 H) 2.20 - 2.31 (m, 1H) 1.91 - 2.02 (m, 1H) 1.78 - 1.89 (m, 1H) 1.66 - 1.77 (m, 8H) 1.28 - 1.40 (m, 2H)	523	6
I-642		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (4- fluoro- fenil)- piridin- 2- ilamina		(400 MHz, DMSO- D_6) d ppm 7.61 (d, J = 1.77 Hz, 1H) 7.38 (dd, J = 8.97, 4.93 Hz, 1H) 7.20 – 7.29 (m, 3H) 6.99 - 7.07 (m, 2H) 6.76 (d, J = 1.77 Hz, 1H) 5.95 (q, J = 6.65 Hz, 1H) 5.70 (s, 2H) 1.62 (d, J = 6.57 Hz, 3H)	395	1
I-643		6'- amino- 5'- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 1H- [3,3']bipiridinil- 6- ona	0.0432	(500 MHz, DMSO- D_6) d ppm 7.73 (s, 1H) 7.73 - 7.46 (m, 5H) 7.09 (d, J = 1.55 Hz, 1H) 6.42 (d, J = 9.5 Hz, 1H) 6.29 (q, J = 6.65 Hz, 1H) 1.84 (d, J = 6.60 Hz, 3H)	394	3
I-644		5'- bromo- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [3,3']bipiridinil- 6- ona	0.1958	(300 MHz, CDCl3D1) d ppm 8.54 (d, 2H) 7.80 (m, 2H) 7.33 (m, 1H) 7.08 (m, 1H) 6.93 (s, 1H) 6.12 (q, J = 6.7 Hz, 1H) 5.041 (br, s, 2H) 1.88 (d, J = 6.7 Hz, 3H)	458 [M+2]	3
I-645		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (4- dimetilamino- fenil)- piridin- 2- ilamina	0.1572	(300 MHz, CDCl3D1) d ppm 7.83 (d, J = 1.87 Hz, 1H) 7.28 (m, 4H) 7.04 (m, 1H) 6.98 (d, J = 1.76 Hz, 1H) 6.75 (m, 2H) 6.11 (q, J = 6.7 Hz, 1H) 4.76 (br. s, 2H) 2.97 (s, 6H) 1.85 (d, J = 6.7 Hz, 3H)	420	3
I-646		5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 2'- metoxi- [3,3']bipiridinil- 6- ilamina	0.099	(300 MHz, CDCl3D1) d ppm 8.10 (s, 1H) 7.77 (s, 1H) 7.50 (m, 1H) 7.30 (m, 1H) 7.09 (m, 2H) 6.92 (m, 1H) 6.00 (d, J = 6.7 Hz, 1H) 4.91 (br. s, 2H) 3.87 (s, 3H) 1.83 (d, J = 67 Hz, 3H)	MS 408 m/z	3
I-647		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (1H- indol- 5- il)- piridin- 2- ilamina	0.1664	(300 MHz, CDCl3D1) d ppm 8.21 (s, 1H) 7.93 (m, 1H) 7.64 (m, 1H) 7.43 (m, 1H) 7.32 - 7.21 (m, 3H) 7.09 - 7.024 (m, 2H) 6.58 (m, 1H) 6.16 (m, 1H) 4.80 (s, 2H) 3.50 (s, 2H) 1.87 (d, J = 8.69 Hz, 3H)	416	3

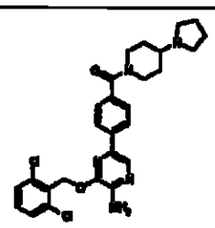
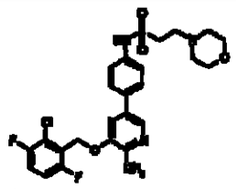
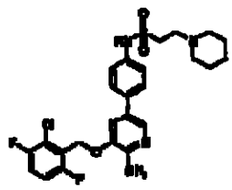
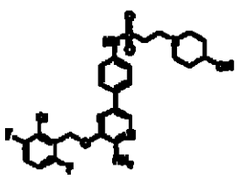
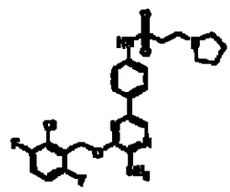
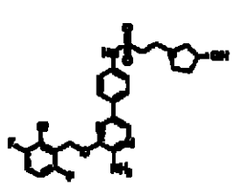
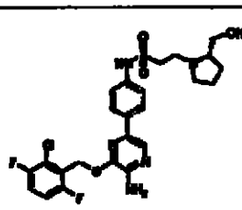
No.	Estructura	Nombre	Ki (μM) o I (%)	^{1}H- NMR	Ms m/z (M+H)	Procedimiento
I-648		(4- {6- amino- 5- [1- (2,6- dicloro- fenil)- propoxi]- piridin- 3- il}- fenil)- (3,5- dimetil- piperazin- 1- il)- metanona	0.5533	(300 MHz, CDCl3D1) d ppm 7.87 (s, 1H) 7.42 (m, 4 H) 7.30 (m, 3H) 7.16 (m, 1H) 7.05 (s, 1H) 5.92 (m, 1H) 4.97 (s, 2H) 4.61 (br. s, 1H) 3.65 (br. s, 2H) 2.85 (br. s, 3H) 2.49 (br. s, 1H) 2.41 (m, 3H) 2.19 (m, 1H) 1.08 (m, 6H)	513	1
I-649		[4- (6- amino- 5- benciloxi- piridin- 3- il)- fenil]- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	29%	(400 MHz, DMSO- D_6) d ppm 7.92 (d, J = 1.77 Hz, 1H) 7.68 (d, J = 8.34 Hz, 2H) 7.53 (d, J = 7.07 Hz, 2H) 7.37 - 7.46 (m, 5H) 7.33 (m, 1H) 5.96 (s, 2H) 5.25 (s, 2H) 3.49 (s 2H) 3.09 (s, 2H) 2.00 (s, 2H) 1.84 (s, 2H) 1.56 (s, 1H)	457	1
I-650		3- (2,6- dicloro- 3- fluoro- benciloxi)- 5- tiazol- 2- il- piridin- 2- ilamina	0.3627	(300 MHz, CDCl3- D1) d ppm 8.25 (d, J = 1.79 Hz, 1H) 7.76 (d, J = 3.30 Hz) 7.36 - 7.26 (m, 3H) 7.20 (m, 1H) 7.05 (m, 1H) 6.17 (q, J = 6.7 Hz, 1H) 6.09 (br. s, 2H) 1.86 (d, J = 6.7 Hz 3H)	384	37
I-651		(4- {6- amino- 5- [1- (2- fluoro- 6- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	1.5258	(400 MHz, DMSO- D_6) d ppm 7.93 (d, J = 1.52 Hz, 1H) 7.74 - 7.82 (m, 3H) 7.71 (m, 3H) 7.62 - 7.67 (m, 3H) 7.47 (m, 4 H) 7.38 (m, 1H) 5.43 (s, 2H) 3.67 (br. s, 2H) 3.51 (br. s, 3H) 3.40 (br. s, 1H) 3.09 (br. s, 2H) 2.00 (br. s, 3H) 1.83 (br. s, 2H) 1.53 (br. s, 2H)	533	6
I-652		3- (2,6- dicloro- 3- fluoro- benciloxi)- 5- (1- metil- 1H- imidazol- 2- il)- piridin- 2- ilamina	11%	(300 MHz, CDCl3- D1) d ppm 7.90 (d, J = 1.67 Hz, 1H) 7.30 (m, 2H) 7.05 (m, 3H) 6.91 (d, J = 0.98 Hz, 1H) 6.10 (q, J = 6.7 Hz, 1H) 4.99 (br. s, 2H) 3.57 (s, 3H) 1.83 (d, J = 6.7 Hz, 3H)	381	38
I-653		{4- [6- amino- 5- (2,4,6- trimetil- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	2%	(400 MHz, DMSO- D_6) d ppm 7.92 (s, 1H) 7.90 (s, 1H) 7.84 (d, J = 8.34 Hz, 2H) 7.50 (d, J = 8.34 Hz, 2H) 6.92 (s, 2H) 5.27 (s, 2H) 3.51 (br. s, 8H) 3.09 (br. s, 3H) 2.32 (s, 8 H) 2.25 (s, 3H) 1.99 (br. s, 2H) 1.84 (br. s, 2H) 1.53 (br. s, 2H)	499	6
I-654		{4- [6- amino- 5- (2,3,5,6- tetrametil- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	9%	(400 MHz, DMSO- D_6) d ppm 9.75 (s, 1H) 7.88 (s, 2H) 7.79 (d, J = 8.34 Hz, 2H) 7.45 (d, J = 8.08 Hz, 3H) 6.97 (s, 1H) 5.28 (s, 2H) 3.64 (s, 1H) 3.45 (s, 2H) 3.34 (s, 1H) 3.04 (s, 3H) 2.15 (s, 12H) 1.94 (s, 3H) 1.79 (s, 2H) 1.50 (s, 2H)	513	6
I-655		{4- [6- amino- 5- (2,4,6- trifluoro- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona		(400 MHz, DMSO- D_6) d ppm 7.83 (d, J = 2.02 Hz, 1H) 7.48 (d, J = 8.34 Hz 3H) 7.33 (d, J = 8.34 Hz, 3H) 7.24 (d, J = 1.77 Hz, 1H) 7.12 - 7.22 (m, 2H) 5.86 (m, 1H) 5.76 (s, 2H) 4.19 (br. s, 1H) 3.55 (br. s, 1H) 2.96 (br. s, 2H) 2.16 (br. s, 1H) 1.83 (br. s, 2H) 1.69 (br. s, 5H) 1.60 (d, J = 5.67 Hz, 5H) 1.30 (br. s, 2H)	525	6
I-656		(4- {6- amino- 5- [1- (2- fluoro- 6- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona		(400 MHz, DMSO- D_6) d ppm 7.89 (d, J = 1.77 Hz, 1H) 7.57 - 7.65 (m, 3H) 7.41 - 7.49 (m, 2H) 7.36 (d, J = 8.08 Hz, 2H) 7.19 (d, J = 1.77 Hz, 1H) 5.85 (s, 2H) 5.80 (s, 1H) 4.21 (s, 1H) 3.57 (br. s, 1H) 3.02 (s, OH) 2.22 (s, 1H) 1.80 (br. s, 2H) 1.78 (d, J = 6.3 Hz, 3H) 1.66 (s, 4H) 1.34 (s, 2H)	557	6

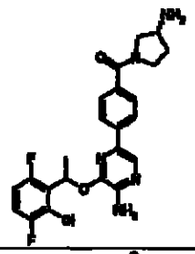
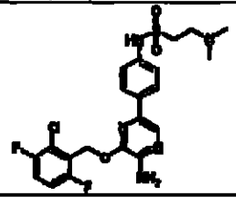
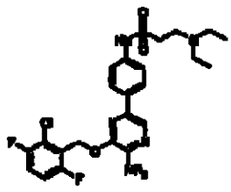
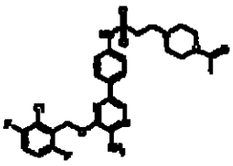
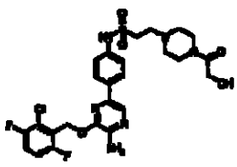
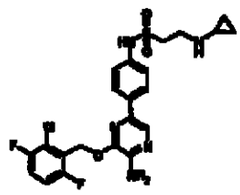
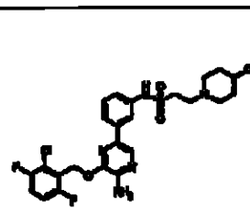
No.	Estructura	Nombre	Ki (μM) o I (%)	^{1}H- NMR	Ms m/z (M+1)	Procedimiento
I-657		6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- N- metil- nicotinamidina		(400 MHz, DMSO- D_6) δ ppm 8.82 (br. s, 1H) 7.97 (d, J = 1.77 Hz, 1H) 7.52 – 7.57 (m, 1H) 7.46 (t, J = 8.72 Hz, 1H) 7.05 (d, J = 1.26 Hz, 1H) 6.73 (br. s, 1H) 6.06 (quart., J = 6.57 Hz, 1H)2, 91 (s, 3H) 1.78 (d, J = 6.57 Hz, 3H)	357	39
I-658		6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- N- (2- morfolin- 4- il- etil)- nicotinamidina		(400 MHz, DMSO- D_6) δ ppm 9.07 (br. s, 1H) 7.94 (d, J = 1.52 Hz, 1H) 7.53 (m, 1H) 7.47 (m, 1H) 6.97 (s, 1H) 6.77 (br. s, 1H) 6.06 (s, 1 H) 3.55 (quart. J 4.29 Hz, 2H) 3.54 (m, 2H) 3.47(m, 2H) 2.54 (t, J = 6.06 Hz, 2H) 2.42 (s, 3H) 1.78 (d, J = 6.82 Hz, 3H)	456	39
I-659		(4- {6- amino- 5- [1- (2,4,5- trifluoro- fenil)- propoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona		(400 MHz, DMSO- D_6) d ppm 9.84 (s, 1H) 7.91 (d, J = 1.52 Hz, 1H) 7.78 - 7.88 (m, 1H) 7.65 - 7.75 (m, 3H) 7.57 (dd, J = 10.23, 3.66 Hz, 1H) 7.46 (d, J = 8.34 Hz, 2H) 5.91 - 5.98 (m, 1H) 3.50 (s, 2H) 3.40 (s, 1H) 3.09 (s, 2H) 2.09 (dt, J =14.08, 6.98 Hz, 2H) 1.99 (s, 2H) 1.92 (dt, J = 13,90, 6,95 Hz, 2H) 1.83 (s, 2H) 1.55 (s, 2H) 0.92 (t, J =7.33 Hz, 3H)	540	6
I-660		(4- {6- amino- 5- [1- (6- cloro- 2- fluoro- 3- metil- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona		NMR (400 MHz, DMSO- D_6) d ppm 9.84 (s, 1H) 7.95 (s, 2H) 7.65 (d, J = 8.34 Hz, 2H) 7.53 - 7.60 (m, 2H) 7.48 (s, 1H) 7.32 - 7.42 (m, 2H) 6.25 (q, J = 6.48 Hz, 1H) 3.58 (s 2H) 3.49 (s 1H) 3.18 (d, J = 5.05 Hz, 3H) 2.27 (d, J =1.52 Hz, 5H) 2.01 - 2.13 (m, 4H) 1.89 (d, J = 6.57 Hz, 5H) 1.64 (d, 2H)	539	6
I-661		ácido 3- (1- {2- amino- 5- [4- (4- pirrolidin- 1- il- piperidina- 1- carbonil)- fenil]- piridin- 3- iloxi}- etil)- benzoico		(400 MHz, DMSO- D_6) d ppm 10.14 (s, 1H) 8.12 (s, 1H) 7.93 (s, 1H) 7.76 - 7.87 (m, 4H) 7.72 (s, 1H) 7.65 (d, J = 8.34 Hz, 2H) 7.53 (ddd, J = 15.92, 7.83, 7.58 Hz, 2H) 7.40 – 7.47 (m, 3H) 6.03 - 6.10 (m, 1H) 4.55 (s, 1H) 3.64 (s, 1H) 3.47 (s, 2H) 3.38 (s, 1H) 3.07 (s, 3H) 2.13 (s, 1H) 1.98 (s, 3H) 1.78 - 1.89 (m, 3H) 1.65 (t, J = 5.68 Hz, 3H) 1.56 (s, 2H) 1.31 (d, J = 6.57 Hz, 2H)	516	6

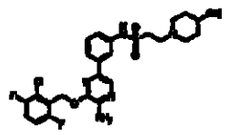
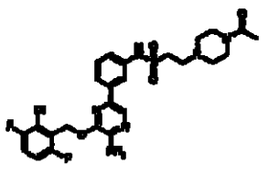
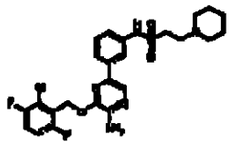
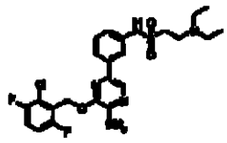
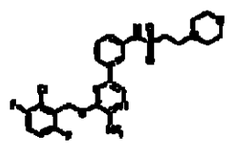
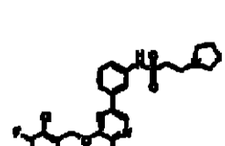
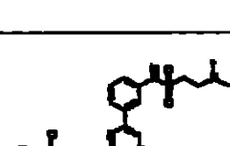
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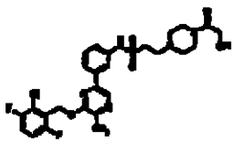
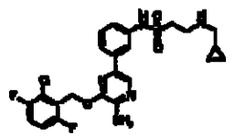
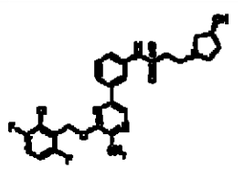
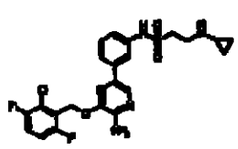
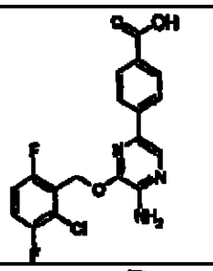
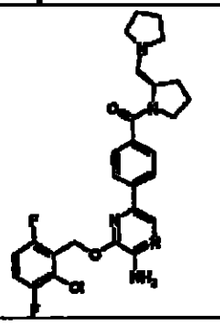
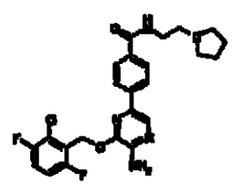
Tabla 4

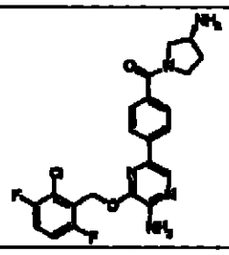
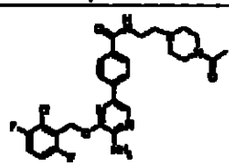
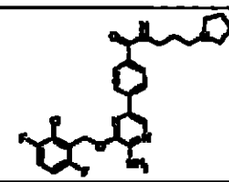
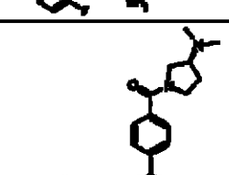
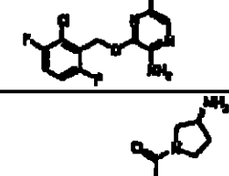
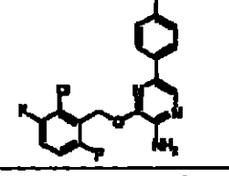
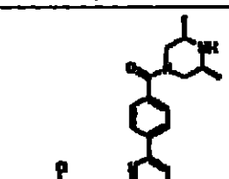
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 1		4- [5- amino- 6- (2,6dicloro- benciloxi)- pirazin- 2- il]- fenol	1.35	ver ejemplo	(400 MHz, DMSO- d_6) δ 5.61 (s, 2H), 6.09 (s, 2H), 6.79 (d, 2H), 7.45 (t, 1H), 2.56 (d, 2H), 7.76 (d, 2H), 7.99 (s, 1H) 9.46 (s, . 1H)	362
II- 2		3- (2,6- dicloro- benciloxi)- 5- [4- (1,1- dioxo- 1λ^6- oxotiazolidin- 2- il)- fenil]- pirazin- 2- ilamina	0.825	ver ejemplo	(400 MHz, DMSO- d_6) δ 2.41 (m, 2H), 3.51 (m, 2H), 3.76 (m, 2H), 5.62 (s, 2H), 6.28 (s, 2H), 7.22 (m, 2H), 7.48 (m, 1H), 7.56 (m, 2H), 7.94 (m, 2H), 8.14 (s, 1H)	465
II- 3		3- (2,6- dicloro- benciloxi)- 5- [3- (2- morpholin- 4- il- etoxi)- phenil]- pirazin- 2- ilamina	0.74	ver ejemplo	(400 MHz, DMSO- d_6) δ 2.45 (m, 4H), 2.71 (t, 2H), 3.56 (t, 4H), 4.15 (t, 2H), 5.61 (s, 2H), 6.32 (s, 2H), 6.86 (d, 1H), 7.29 (t, 1H), 7.46 (m, 2H), 7.52 (m, 1H), 7.55 (s, 1H), 7.57 (d, 1H), 8.16 (s, 1H)	475
II- 4		3- (2,6- dicloro- benciloxi)- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- pirazin- 2- ilamina	1.25	ver ejemplo	(400 MHz, DMSO- d_6) δ 2.45 (m, 4H), 2.71 (m, 2H), 3.59 (t, 4H), 4.11 (t, 2H), 5.64 (s 2H), 6.18 (s, 2H), 6.97 (d, 2H), 7.46 (t, 1H), 7.56 (d, 2H), 7.86 (d, 2H), 8.06 (s, 1H)	475
II- 5		5- (4- amino- fenil)- 3- (2,6- dicloro- benciloxi)pirazin- 2- ilamina	0.94	ver ejemplo	(400 MHz, DMSO- d_6) δ 5.19 (s, 2H), 5.59 (s, 2H), 5.96 (s, 2H), 6.60 (d, 2H), 7.45 (t. 1H), 7.56 (d, 2H), 7.62 (d, 2H), 7.91 (s, 1H)	361
II- 6		acido 4- [5- amino- 6- (2,6dicloro- benciloxi)- pirazin- 2- il]- benzoico	1.75	ver ejemplo	(400 MHz, DMSO- d_6) δ 5.64 (s, 2H), 6.52 (s, 2H), 7.46 (m, 1H), 7.56 (m, 2H), 7.96 (d, 2H), 8.07 (d, 2H), 8.27 (s, 1H)	390
II- 7		{4- [5- amino- 6- (2,6- dicloro- benciloxi)- pirazin- 2- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidil- 1- il]- metanona	0.24	ver ejemplo	(400 MHz, DMSO- d_6) δ 1.79 (m, 10H), 2.64 (m, 4H), 3.45 (m, 3H), 5.64 (s, 2H), 6.42 (s, 2H), 7.49 (m, 3H), 7.58 (m, 2H), 7.98 (d, 2H), 8.00 (s, 1H)	526

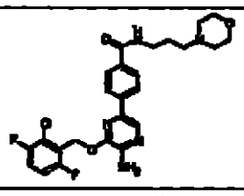
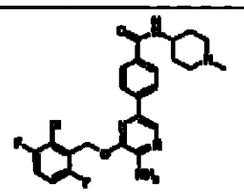
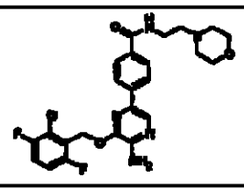
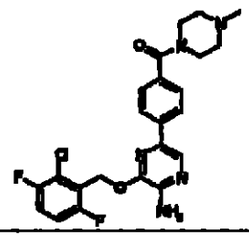
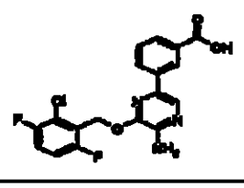
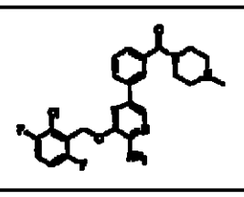
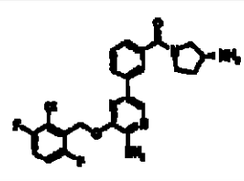
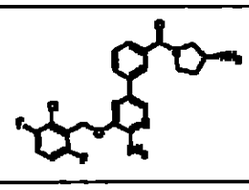
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 8		{4- [5- amino- 6- (2,6- dicloro- benciloxi)- pirazin- 2- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	0.56	ver ejemplo	(400 MHz, DMSO- d_6) δ 1.37 (m, 2H), 1.66 (m, 4H), 1.85 (m, 2H), 2.32 (m, 2H), 2.52 (m, 4H), 3.04 (m, 2H), 3.92 (m, 1H), 5.62 (s, 2H), 6.42 (s, 2H), 7.40 (d, 2H), 7.46 (t, 1H), 7.58 (m, 2H), 8.00(d, 2H), 8.21 (s, 1H)	526
II- 9		ácido 2- morfolin- 4- il- etanosulfonico {4- [5- amino- 6- (2- cloro- 3,6- dicloro- benciloxi)- pirazin- il]fenil}- amida	1.26	ver ejemplo	(300 MHz, $CDCl_3$) δ 12.50 (t, 42H), 2.92 (t, 2H), 3.29 (t, 2H), 3.72 (t, 2H), 4.81 (s, 2H), 5.67 (d, 2H), 7.05 (m, 2H), 7.20 (m, 1H), 7.28 (m, 2H), 7.90 (d, 2H), 8.04 (s, 1H)	540
II- 10		ácido 2- piperidin- 1- il- etanosulfonico {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida	1.2	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.60 (m, 2H), 1.63 (m, 4H), 2.49 (m, 4H), 2.90 (t, 2H), 3.26 (t, 2H), 4.85 (s, 2H), 5.67 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.29 (d, 2H), 7.89 (d, 2H), 8.04 (s, 1H)	538
II- 11		ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfonico {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida	0.65	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.63 (m, 2H), 1.90 (m, 2H), 2.27 (t, 2H), 2.80 (m, 2H), 2.92 (t, 2H), 4.86 (s, 2H), 5.67 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.28 (d, 2H), 7.90 (d, 2H), 8.04 (s, 1H)	554
II- 12		ácido 2- pirrolidin- 1- il- etanosulfonico {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida	0.58	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.83 (m, 4H), 2.56 (m, 4H), 3.04 (t, 2H), 3.28 (t, 2H), 4.91 (s, 2H), 5.67 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.27 (d, 2H), 7.88 (d, 2H), 8.03 (s, 1H)	524
II- 13		ácido 2- [(3R)- 3- hidroxi- pirrolidin- 1- il]- etanosulfonico {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida	1.59	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.85 (m, 1H), 2.25 (m, 2H), 2.55 (m, 1H), 2.84 (d, 1H), 3.02 (m, 3H), 3.26 (m, 2H), 4.43 (m, 1H), 4.82 (s, 2H), 5.67 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.35 (d, 2H), 7.88 (d, 2H), 8.04 (s, 1H)	540
II- 14		ácido 2- [(2S)- 3- hidroximetil- pirrolidin- 1- il]- etanosulfonico {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida	1.78	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.85 (m, 4H), 2.20 (m, 1H), 2.70 (m, 2H), 3.05 (m, 2H), 3.30- 3.70 (m, 3H), 3.95 (m, 1H), 4.79 (s, 2H), 5.67 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.32 (d, 2H), 7.88 (d, 2H), 8.05 (s, 1H)	554

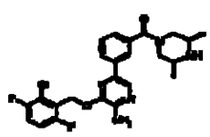
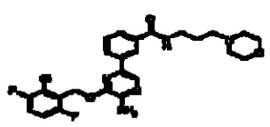
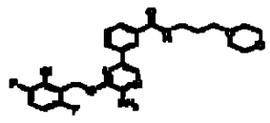
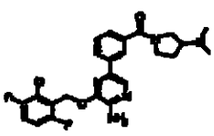
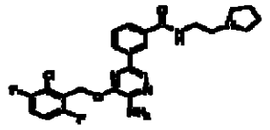
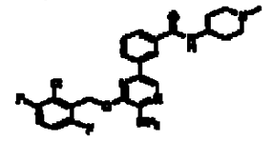
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 15		ácido 2- (ciclopropilmetil- amino) etanosulfonico {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida	1.28	ver ejemplo	^{1}H- NMR (300 MHz, $CDCl_3$) δ 0.14 (m, 2H), 0,52 (m, 2H), 0.95 (m, 1H), 2.50 (d, 2H), 3.21 (m, 4H), 4.86 (s, 2H), 5.67 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.30 (d, 2H), 7.89 (d, 2H), 8.04 (s, 1H)	524
II- 16		ácido 2- dimetilamino- etanosulfonico {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida	0.91	ver ejemplo	(300 MHz, $CDCl_3$) δ 2.30 (s, 6H), 2.86 (t, 2H), 3.21 (t, 2H), 4.83 (s, 2H). 5.67 (d, 2H), 7.05 (m, 1H), 7.18 (m, 1H), 7.28 (d, 2H), 7.88 (d, 2H), 8.05 (s, 1H)	498
II- 17		ácido 2- dietilamino- etanosulfonico {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida	0.46	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.08 (t, 6H), 2.61 (q, 4H), 3.03 (t, 2H), 3.23 (t, 2H), 4.80 (s, 2H), 5.67 (d, 2H), 7.05 (m, 1H), 7.19 (m, 1H), 7.27 (d, 2H), 7.88 (d, 2H), 8.04 (s, 1H)	526
II- 18		ácido 2- (4- acetil- piperacin- 1- il)- etanosulfonico {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida	1.5	ver ejemplo	(300 MHz, $CDCl_3$) δ 2.08 (s, 3H), 2.46 (m, 4H), 2.93 (t, 2H), 3.30 (t, 2H), 3.47 (t, 2H), 3.62 (t, 2H), 4.82 (s, 2H), 5.67 (s, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.28 (d, 2H), 7.91 (d, 2H), 8.05 (s, 1H)	581
II- 19		ácido 2- [4- (2- hidroxi- acetil)- piperacin- 1- il]- etanosulfonico {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida	0.45	ver ejemplo	(300 MHz, $CDCl_3$) δ 2.48 (t, 4H), 2.93 (t, 2H), 3.30 (m, 4H), 3.55 (bm, 1H), 3.67 (t, 2H), 4.14 (s, 2H), 4.84 (s, 2H), 5.67 (s, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.27 (d, 2H), 7.92 (d, 2H), 8.05 (s, 1H)	597
II- 20		ácido 2- ciclopropilamino- etanosulfonico {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida	1.29	ver ejemplo	(300 MHz, $CDCl_3$) δ 0.37 (m, 2H), 2.14 (m, 1H), 3.24 (m, 4H), 4.93 (s, 2H), 5.67 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.28 (d, 2H), 7.90 (d, 2H), 8.03 (s, 1H)	510
II- 21		ácido 2- [(3R)- 3- hidroximetil- pirrolidin- 1- il]- etanosulfonico {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida	1.38	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.60- 2.0 (m, 5H), 2.15 (m, 1H), 2.55- 2.70 (m, 2H), 2.90- 3.15 (m, 2H), 3.3- 3.62 (m, 2H), 3.89 (dd, J = 3.0, 11.3 Hz, 1H), 4.92 (s, 2H), 5.66 (s, 2H), 6.95- 7.60 (m, 5H), 7.55- 7.70 (m, 2H), 7.77 (s, 1H), 8.10 (s, 1H)	554

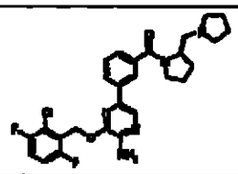
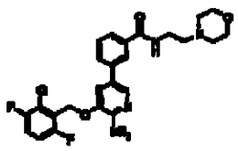
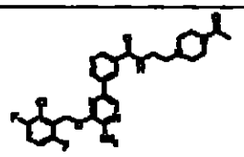
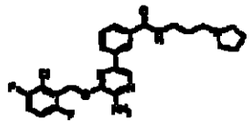
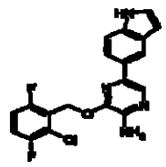
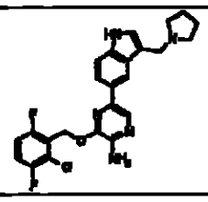
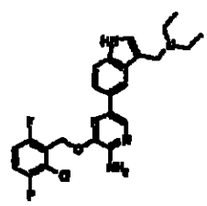
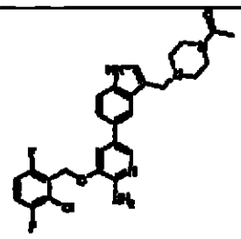
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II-22		ácido 2-(4-hidroxi-piperidin-1-il)-etanosulfonico {3-[5-amino-6-(2-cloro-3,6-difluoro-benciloxi)-pirazin-2-il]-fenil}-amida	0.7	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.40-1.60 (m, 2H), 1.75-1.88 (m, 2H), 2.21 (t, J = 9.0 Hz, 2H), 2.65-2.75 (m, 2H), 2.85-2.95 (m, 2H), 3.20-3.35 (m, 2H), 3.69 (m, 1H), 5.17 (s, 2H), 5.68 (s, 2H), 6.92-7.02 (m, 1H), 7.08-7.20(m, 1H), 7.30-7.45 (m, 2H), 7.69 (s, 1H), 7.76 (d, J = 7.5 Hz, 1H), 8.14 (s, 1H)	555
II-23		ácido 2-(4-acetil-piperidin-1-il)-etanosulfonico {3-[5-amino-6-(2-cloro-3,6-difluoro-benciloxi)-pirazin-2-il]-fenil}-amida	2.79	ver ejemplo	(300 MHz, $CDCl_3$) δ 2.03 (s, 3H), 2.30-2.04 (m, 2H), 2.75-2.85 (m, 2H), 3.20-3.40 (m, 4H), 345-3.55 (m, 2H), 5.35 (s, 2H), 5.68 (s, 2H), 695-7.02 (m, 1H), 7.05-7.20 (m, 1H), 7.30-7.45 (m, 2H), 7.64 (s, 1H), 7.76 (d, J = 7.3 Hz, 1H), 8.13 (s, 1H), 8.52 (s, 1H)	582
II-24		ácido 2-piperidin-1-il-etanosulfonico {3-[5-amino-6-(2-cloro-3,6-difluoro-benciloxi)-pirazin-2-il]-fenil}-amida	3.5	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.30-1.60 (m, 6H), 2.30-2.45 (m, 4H), 2.75-2.90 (m, 2H), 3.15-3.30 (m, 2H), 5.10 (s, 2H), 5.66 (s, 2H), 6.95-7.05 (m, 1H), 7.10-7.20 (m, 1H), 7.25-7.40 (m, 2H), 7.60-7.75 (m, 2H), 8.10 (s, 1H)	539
II-25		ácido 2-dietilamino-etanosulfonico {3-[5-amino-6-(2-cloro-3,6-difluoro-benciloxi)-pirazin-2-il]-fenil}-amida	3.7	ver ejemplo	(300 MHz, $CDCl_3$) δ 0.95-1.05 (m, 6H), 2.45-2.55 (m, 4H), 2.95-3.10 (m, 2H), 3.15-3.25 (m, 2H), 5.11 (s, 2H), 5.67 (s, 2H), 6.90-7.15 (m, 2H), 7.20-7.40 (m, 2H), 7.55-7.70 (m, 2H), 8.10 (s, 1H)	527
II-26		ácido 2-morfolin-4-il-etanosulfonico {3-[5-amino-6-(2-cloro-3,6-difluoro-benciloxi)-pirazin-2-il]-fenil}-amida	3.3	ver ejemplo	(300 MHz, $CDCl_3$) δ 2.30-2.50 (m, 2H), 2.80-3.00 (m, 2H), 3.20-3.40 (m, 2H), 3.50-3.75 (m, 4H), 5.21 (s, 2H), 5.67 (s, 2H), 6.95-7.08 (m, 1H), 7.10-720 (m, 1H), 7.30-7.50 (m, 2H), 7.67 (s, 1H), 7.74 (d, J = 7.5 Hz, 1 H) 8.12 (s, 1H)	541
II-27		ácido 2-pirrolidin-1-il-etanosulfonico {3-[5-amino-6-(2-cloro-3,6-difluoro-benciloxi)-pirazin-2-il]-fenil}-amida	1.8	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.62-1.82 (m, 4H), 2.40-2.55 (m, 4H), 292-3.00 (m, 2H), 3.25-3.35 (m, 2H), 5.24 (s, 2H), 5.67 (s, 2H), 6.95-7.08 (m, 1H), 7.10-720 (m, 1H), 7.25-7.40 (m, 2H), 7.63 (s, 1H), 7.73 (d, J = 7.1 Hz, 1 H) 8.12 (s, 1H)	525
II-28		ácido 2-dimetilamino-etanosulfonico {3-[5-amino-6-(2-cloro-3,6-difluoro-benciloxi)-pirazin-2-il]-fenil}-amida	2.28	ver ejemplo	(300 MHz, $CDCl_3$) δ 2.27 (s, 6H), 2.86 (t, J = 6.4 Hz, 2H), 3.23 (t, J = 6.4 Hz, 2H), 5.08 (s, 2H), 5.67 (s, 2H), 7.00-7.45 (m, 4H), 7.65-7.75 (m, 2H), 8.11 (s, 1H)	499

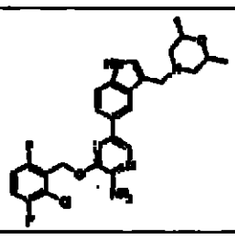
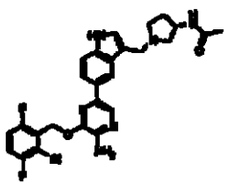
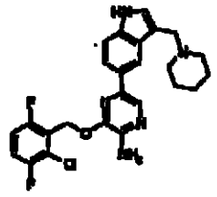
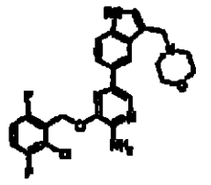
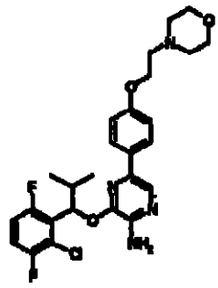
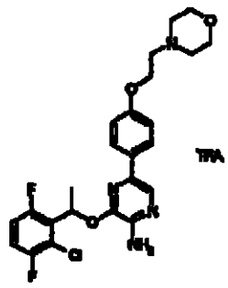
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 29		ácido 2- [4- (2- hidroxi- acetil)- piperidin- 1- il]- etanosulfonico {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida	1.82	ver ejemplo	(300 MHz, $CDCl_3$) δ 2.43 (t, 4H), 2.92 (t, 2H), 3.20 (t, 2H), 3.33 (t, 2H), 3.54 (br s, 1H), 3.61 (t, 2H), 4.08 (s, 2H), 5.18 (br s. 2H), 5.67 (s, 2H), 7.00- 7.45 (m, 4H), 7.65- 7.75 (m, 2H), 8.11 (s, 1H)	597
II- 30		ácido 2- (ciclopropilmetil- amino)- etanosulfonico {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida	1.84	ver ejemplo	(300 MHz, $CDCl_3$) δ 0.07 (m, 2H), 0.44 (m, 2H), 0.89 (m, 1H), 2.45 (d, 2H), 3.16 (t, 2H), 3.29 (t, 2H), 5.27 (br s, 2H), 5.67 (s, 2H), 7.07 (m, 1H). 7.20 (m, 1H), 7.41 (m, 2H), 7.65 (s, 1H), 7.77 (m, 1H), 8.12 (s, 1H)	524
II- 31		ácido 2- [(3R)- 3- hidroxi- pirrolidin- 1- il]- etanosulfonico {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida	2.16	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.80 (m, 1H), 2.20 (m, 2H), 2.50 (m, 1H), 2.70- 3.20 (m, 5H), 3.32 (m, 2H), 4.35 (m, 1H), 5.12 (s, 2H), 5.68 (s, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.40 (m, 2H), 7.73 (m, 2H), 8.15 (s, 1H)	540
II- 32		ácido 2- ciclopropilamino- etanosulfonico {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida	2.13	ver ejemplo	(300 MHz, $CDCl_3$) δ 0.25- 0.50 (m, 4H), 2.09 (m, 1H), 3.15- 3.40 (m, 4H), 5.37 (s, 2H), 5.68 (s, 2H), 7.07 (m, 1H), 7.18 (m, 1H), 7.42 (m, 2H), 7.62 (m, 1H), 7.77 (m, 1H), 8.13 (s, 1H)	510
II- 33		4- [5- amino- 6- (2- cloro- 3,6 difluoro- benciloxi)- pirazin- 2- il]- ácido benzoico		ver ejemplo		392
II- 34		{4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona	0.15	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.5- 2.2 (m, 10H), 2.65 (m, 4H), 3.50 (m, 2H), 4.42 (m, 1H), 4.86 (br s, 2H), 5.68 (d, J = 1.3 Hz, 2H), 7.05 (m, 1H), 7.19 (m, 1H), 7.57 (m, 2H), 7.96 (d, 2H), 8.12 (s, 1H)	528
II- 35		4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (2- pirrolidin- 1- il- etil)- benzamida	0.13	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.87 (m, 4H), 2.78 (m, 4H), 2.85 (t, 2H), 3.61 (m, 2H), 4.91 (s, 2H), 5.68 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.89 (d, 2H), 7.99 (d, 2H), 8.13 (s, 1H)	489

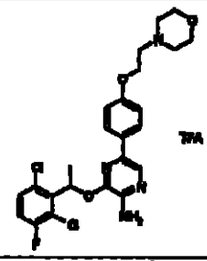
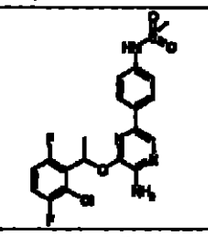
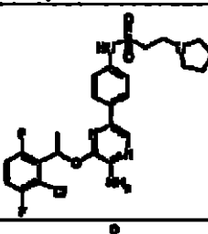
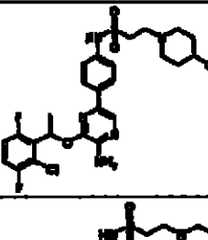
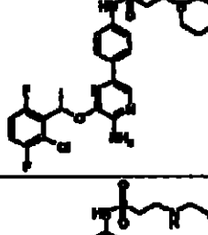
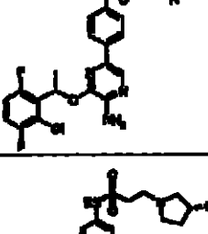
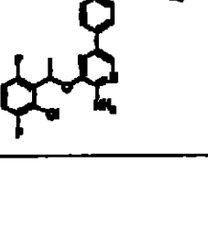
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 36		{4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il]- metanona	0.37	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.80- 240 (m, 2H), 2.24 (s, 3H), 3.30- 3.90 (m, 5H), 5.71 (s, 2H), 7.25 (m, 1H), 7.35 (m, 1H), 7.60 (m, 2H), 8.03 (d, 2H), 8.10 (s, 1H)	461
II- 37		N- [2- (4- acetil- piperacin- 1- il)- etil]- 4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- benzamida	1.35	ver ejemplo	(300 MHz, $CDCl_3$) δ 2.10 (s, 3H), 2.52 (m, 4H), 2.66 (t, 2H), 3.40- 3.80 (m, 6H), 4.94 (s, 2H), 5.68 (s, 2H), 6.75 (bra, 1H), 7.05 (m, 1H), 7.20 (m, 1H), 7.84 (d, 2H), 8.00 (d, 2H) 8.14 (s, 1H)	545
II- 38		4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (3- pirrolidin- 1- il- propil)- benzamida	0.58	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.91 (m, 6H), 2.72 (m, 4H), 2.82 (t, 2H), 3.61 (m, 2H), 4.93 (s, 2H), 5.69 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.89 (d, 2H), 7.97 (d, 2H), 8.12 (s, 1H), 8.73 (s, 1H)	503
II- 39		{4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona	0.67	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.70- 2.10 (m, 1H), 2.24 (s, 3H), 2.34 (s, 3H), 2.60- 2.90 (m, 1H), 3.30- 4.00 (m, 4H), 4.90 (s, 2H), 5.68 (d, 2H), 7.10 (m, 1H), 7.20 (m, 1H), 7.60 (m, 2H), 7.97 (d, 2H), 8.13 (s, 1H)	489
II- 40		{4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3R)- 3- dimetilamino- pirrolidin- 1- il]- metanona	0.46	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.80- 2.40 (m, 2H), 2.24 (s, 3H), 3.30- 3.90 (m, 5H), 5.71 (s, 2H), 7.25 (m, 1H), 7.35 (m, 1H), 7.60 (m, 2H), 8.03 (d, 2H), 8.10 (s, 1H)	461
II- 41		{4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- (3,5- dimetil- piperacin- 1- il)- metanona	0.48	ver ejemplo	(300 MHz, $CDCl_3$) δ 0.9- 1.2 (m, 6H), 2.2- 3.2 (m, 6H), 4.91 (s, 2H), 5.68 (s, 2H), 7.10 (m, 1H), 7.20 (m, 1H), 7.48 (d, 2H), 7.97 (d, 2H), 8.12 (s, 1H)	489
II- 42		{4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)metanona	0.33	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.60- 3.40 (m, 17H), 4.89 (s, 2H), 5.68 (d, 2H), 7.10 (m, 1H), 7.20 (m, 1H), 7.47 (d, 2H), 7.96 (d, 2H), 8.11 (s, 1H)	528

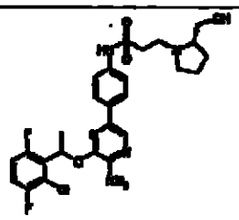
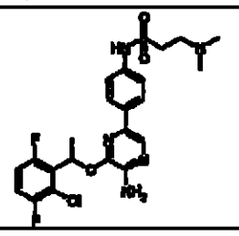
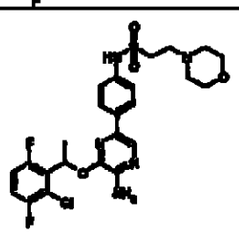
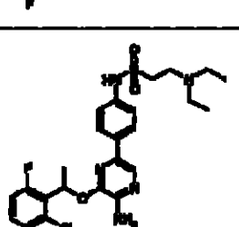
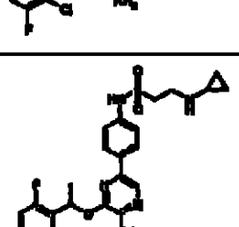
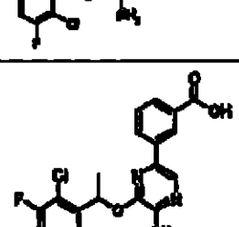
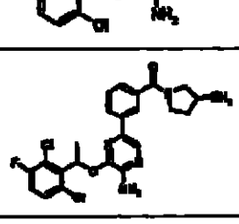
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 43		4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (3- morfolin- 4- il- propil)- benzamida	0.59	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.83 (m, 2H), 2.60 (m, 6H), 3.61 (m, 2H), 3.76 (m, 4H), 4.93 (s, 2H), 5.70 (d, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.88 (d, 2H), 8.00 (d, 2H), 8.14 (s, 1H)	518
II- 44		4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (1- metil- piperidin- 4- il)- benzamida	0.5	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.80 (m, 2H), 2.07 (m, 2H), 2.22 (m, 2H), 2.34 (s, 3H), 2.88 (m, 2H), 4.04 (m, 2H),4.92 (s, 2H), 5.69 (d, 2H), 6.03 (d, 1H), 7.05 (m, 1H), 7.20 (m, 1H), 7.82 (d, 2H), 7.98 (d, 2H), 8.13 (s, 1H)	489
II- 45		4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (2- morfolin- 4- il- etil)- benzamida	1.11	ver ejemplo	(300 MHz, $CDCl_3$) δ 2.68 (m, 6H), 3.60 (m, 2H), 3.75 (m, 4H), 5.72 (s, 2H), 7.25 (m, 1H), 7.35 (m, 1H), 7.88 (d, 2H), 8.05 (d, 2H), 8.12 (s, 1H)	504
II- 46		{4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- (4- metil- piperacin- 1- il)- metanona	0.68	ver ejemplo	(300 MHz, $CDCl_3$) δ 2.39 (s, 3H), 2.48 (m, 4H), 3.69 (m, 4H), 4.89 (s, 2H), 5.69 (s, 2H), 7.08 (m, 1H), 7.20 (m, 1H), 7.52 (d, 2H), 7.95 (d, 2H) 8.08 (s, 1H)	474
II- 47		acido 3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- benzoico		ver ejemplo		392
II- 48		{3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- (4- metil- piperacin- 1- il]- metanona	2.85	ver ejemplo	(300 MHz, $CDCl_3$) δ 2.33 (s, 3H), 2.46 (m, 4H), 3.68 (m, 4H), 4.86 (br s, 2H), 5.67 (s, 2H), 7.08 (m, 1H), 7.20 (m, 1H), 7.35 (d, 1H), 7.47 (t, 1H), 7.95 (m, 2H), 8.10 (s, 1H)	474
II- 49		{3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3R)- 3- amino- pirrolidin- 1- il]- metanona	1.02	ver ejemplo	(300 MHz, $CDCl_3$) δ 2.12 (m, 1H), 2.44 (m, 1H), 3.52- 4.05 (m, 5H), 5.71 (s, 2H), 7.24 (m, 1H), 7.38 (m, 1H), 7.54 (m, 2H), 8.02 (d, 2H), 8.12 (m, 2H)	460
II- 50		{3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il]- metanona	0.91	ver ejemplo	(300 MHz, $CDCl_3$) δ 2.12 (m, 1H), 2.44 (m, 1H), 3.52- 4.05 (m, 5H), 5.71 (s, 2H), 7.24 (m, 1H), 7.38 (m, 1H), 7.54 (m, 2H), 8.02 (d, 2H), 8.12 (m, 2H)	460

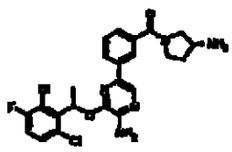
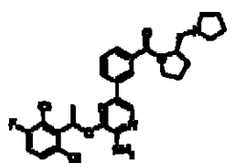
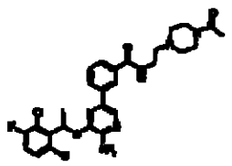
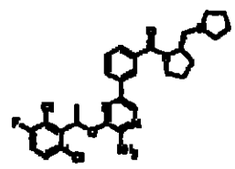
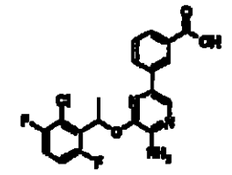
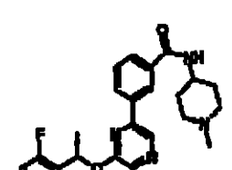
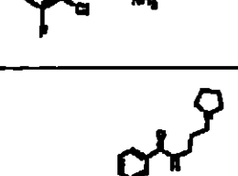
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 51		{3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona	2.56	ver ejemplo	(300 MHz, $CDCl_3$) δ 0.99 (br s, 3H), 1.15 (br s, 3H), 2.42 (m, 1H), 2.70 (m, 1H), 2.84 (m, 1H), 2.93 (m, 1H), 3.66 (m, 1H), 4.67(m, 1H), 4.92 (br s, 2H), 5.66 (s, 2H), 7.05 (m, 1H), 7.20 (m, 1H), 7.35 (m, 1H), 7.47 (t, 1H), 7.97 (m, 2H), 8.10 (s, 1H)	488
II- 52		3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (3- morfolin- 4- il- propil)- benzamida	4.2	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.82 (m, 2H), 2.50- 2.56 (m, 2H), 3.67 (m, 6H), 4.88 (br s, 2H), 5.68 (s, 2H), 7.05 (m, 1H), 7.19 (m, 1H), 7.48 (t, 2H), 7.70 (d, 1H), 7.90 (m, 1H), 8.06 (d, 1H), 8.14 (s, 1H), 8.36 (t, J = 1.6 Hz, 1H)	519
II- 53		{3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	0.83	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.60 (m, 2H), 1.80 (m, 4H), 1.86 (m, 2H), 2.00 (m, 2H), 2.32 (m, 1H), 2.61 (m, 4H), 2.56 (m, 2H), 3.00 (m, 2H), 3.82 (m, 1H),4.66 (m, 1H), 4.93 (br s, 2H), 5.66 (s, 2H), 7.06 (m, 1H), 7.18 (m, 1H), 7.32 (dt, 1H), 7.46 (t, 1H), 7.70 (d, 1H), 7.97 (m, 2H), 8.09 (d, J = 3.6 Hz, 1H)	528
I- 54		{3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona	1.45	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.85 (m, 1H), 2.10 (m, 1H), 2.21 (s, 3H), 2.31 (s, 3H), 2.75 (m, 1H), 3.42 (m, 1H), 3.64 (m, 2H), 3.92 (m, 1H), 4.93 (br s, 2H), 5.67 (s, 2H), 7.06 (m, 1H), 7.18 (m, 1H), 7.46 (m, 2H), 7.97 (m, 1H), 8.09 (m, 2H)	488
II- 55		3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (2- pirrolidin- 1- il- etil)- benzamida	1.6	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.82 (m, 1H), 2.69 (m, 4H), 2.84 (m, 2H), 3.65 (m, 2H), 4.93 (br s, 2H), 5.68 (s, 2H), 7.06 (m, 1H), 7.18 (m, 1H), 7.22 (m, 1H), 7.49 (t, J = 7.7 Hz, 1H), 7.77 (d, J = 7.8 Hz, 1H), 8.06 (dt, J = 7.9 Hz, 1.5 Hz 1H), 8.13 (s, 1H), 8.38 (t, J = 1.5 Hz, 1H)	488
II- 56		3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (1- metil- piperidin- 4- il)- benzamida	0.9	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.71 (m, 2H), 2.11 (m, 2H), 2.28 (t, 2H), 2.95 (m, 2H), 4.11 (m, 1H), 4.89 (s, 2H), 5.69 (s, 1H), 6.28 (m, 1H), 7.08 (m, 1H), 7.18 (m, 1H), 7.45 (t, 1H), 7.68 (d, 1H), 8.06 (d, 1H), 8.11 (s, 1H), 8.35 (s, 1H	488

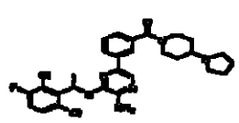
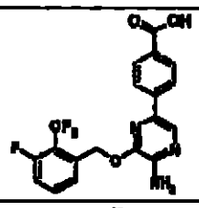
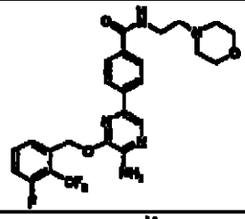
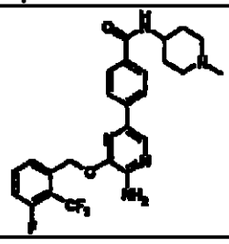
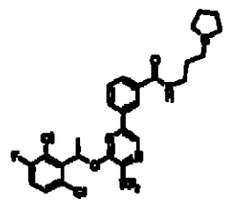
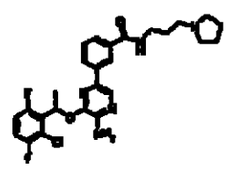
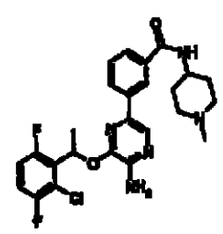
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II-57		3-[5-amino-6-(2-cloro-3,6-difluoro-benciloxi)-pirazin-2-il]-N-(1-metil-piperidin-4-il)-benzamida	0.63	ver ejemplo	(300 MHz, $CDCl_3$) δ 2.02 (m, 10H), 2.75 (m, 4H), 3.42 (m, 2H), 4.51 (m, 1H), 4.86 (s, 2H), 5.69 (s, 2H), 7.08 (m, 1H), 7.20 (m, 1H), 7.48 (m, 2H), 7.98 (m, 1H), 8.07 (m, 1H), 8.11 (s, 1H)	528
II-58		3-[5-amino-6-(2-cloro-3,6-difluoro-benciloxi)-pirazin-2-il]-N-(2-morfolin-4-il-etil)-benzamida	2.5	ver ejemplo	(300 MHz, $CDCl_3$) δ 2.51 (m, 4H), 2.65 (t, 2H), 3.58 (t, 2H), 3.69 (m, 4H), 5.72 (s, 2H), 7.20 (m, 1H), 7.35 (m, 2H), 7.52 (t, 1H), 7.76 (d, 1H), 8.12 (m, 2H), 8.41 (s, 1H)	504
II-59		N-[2-(4-acetil-piperacin-1-il)-etil]-3-[5-amino-6-(2-cloro-3,6-difluoro-benciloxi)-pirazin-2-il]-benzamida	2.77	ver ejemplo	(300 MHz, $CDCl_3$) δ 2.08 (s, 3H), 2.59 (m, 6H), 3.57 (m, 6H), 5.71 (s, 2H), 7.21 (m, 1H), 7.37 (m, 2H), 7.50 (t, 1H), 7.75 (d, 1H), 8.08 (m, 2H), 8.39 (s, 1H)	545
II-60		3-[5-amino-6-(2-cloro-3,6-difluoro-benciloxi)-pirazin-2-il]-N-(2-pirrolidin-1-il-propil)-benzamida	1.48	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.79 (m, 4H), 1.88 (t, 2H), 2.65 (m, 4H), 2.78 (t, 2H), 3.65 (m, 2H),4.86 (s, 2H), 5.69 (s, 2H), 7.06 (m, 1H), 7.21 (m, 1H), 7.45 (t, 1H), 7.68 (d, 1H), 8.06 (d, 1H), 8.16 (s, 1H), 8.40 (s, 1H), 8.69 (m, 1H)	502
II-61		3-(2-cloro-3,6-difluoro-benciloxi)-5-(1H-indol-5-il)-pirazin-2-ilamina		ver ejemplo		387
II-62		3-(2-cloro-3,6-difluoro-benciloxi)-5-(3-pirrolidin-1-ilmetil-1H-indol-5-il)-pirazin-2-ilamina	0.35	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.78 (m, 4H), 2.66 (m, 4H), 3.89 (s, 2H), 4.89 (s, 2H) 5.69 (s, 2H), 7.08 (m, 1H), 7.18 (m, 2H), 7.39 (d, 1H), 7.79 (d, 1H), 8.08 (s, 1H), 8.18 (s, 1H), 8.79 (s, 1H)	470
II-63		3-(2-cloro-3,6-difluoro-benciloxi)-5-(3-dietilaminometil-1H-indol-5-il)-pirazin-2-ilamina	0.73	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.11 (m, 6H), 2.69 (m, 4H), 3.80 (s, 2H), 4.69(s, 1H), 5.77 (s, 2H), 7.02 (m, 1H), 7.21 (m, 2H), 7.45 (d, 1H), 7.89 (d, 1H), 8.22 (m, 3H)	472
II-64		1-(4-{5-[5-amino-6-(2-cloro-3,6-difluoro-benciloxi)-pirazin-2-il]-1H-indol-3-ilmetil}-piperacin-1-il)-etanona	1.5	ver ejemplo	(300 MHz, $CDCl_3$) δ 2.08 (s, 3H), 2.55 (m, 4H), 3.45 (m, 2H), 3.64 (m, 2H), 3.81 (s, 2H), 4.78 (s, 2H), 5.71 (s, 2H), 7.08 (m, 1H), 7.18 (m, 2H), 7.31 (d, 2H), 7.79 (d, 1H), 8.04 (s, 1H), 8.22 (s, 1H), 8.49 (s, 1H)	527

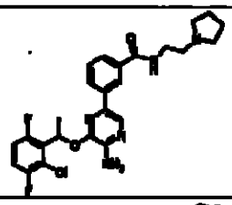
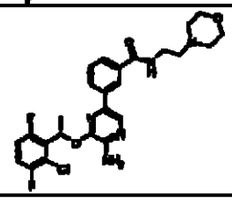
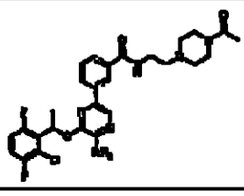
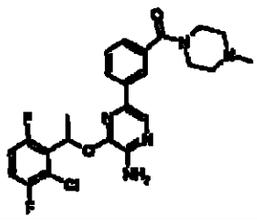
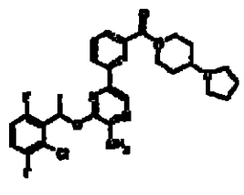
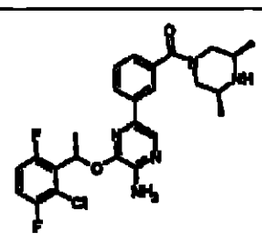
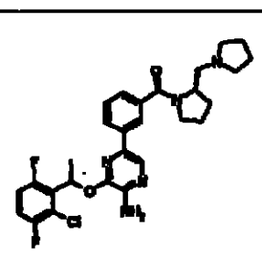
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 65		3- (2- cloro- 3,6- difluoro- benciloxi)- 5- [3- (2,6- dimetil- morfolin- 4- ilmetil)- 1H- indol- 5- il]- pirazin- 2- ilamina	2.4	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.11 (d, 6H), 1.98 (m, 2H), 2.98 (m, 2H), 3.87 (m, 4H), 4.75(s, 2H), 5.78 (s, 2H), 7.08 (m, 1H), 7.27 (m, 2H), 7.48 (d, 1H), 7.89 (d, 1H), 8.19 (s, 1H), 8.28 (s, 2H)	514
II- 66		N- (1- {5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- 1H- indol- 3- ilmetil}- (3S)- pirrolidin- 3- il)- acetamida	0.55	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.69 (m, 1H), 1.88 (s, 3H), 2.39 (m, 2H), 2.75 (m, 2H), 3..08 (m, 1H), 3.95 (m, 2H), 4.50 (m, 1H), 4.79 (s, 2H), 5.78 (s, 2H), 6.01 (m, 1H), 7.05 (m, 1H), 7.18 (m, 2H), 7.42 (d, 1H), 7.79 (d, 1H), 8.12 (s, 1H), 8.12 (s, 1H), 8.28 (s, 1H)	527
II- 67		3- (2- Cloro- 3,6- difluoro- benciloxi)- 5- (3- piperidin- 1- ilmetil- 1H- indol- 5- il)- pirazin- 2- ilamina	0.51	ver ejemplo	(300 MHz, $CDCl_3$) δ 1.49 (m, 2H), 1.71 (m, 4H), 2.66 (m, 4H), 3.89 (s, 2H), 4.79 (s, 2H), 5.69 (s, 2H), 7.08 (m, 1H), 7.18 (m, 1H), 7.31 (s, 1H), 7.42 (d, 1H), 7.78 (d, 1H), 8.08 (s, 1H), 8.18 (s, 1H), 8.69 (br s, 1H)	484
II- 68		3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (3- morfolin- 4- ilmetil- 1H- indol- 5- il)- pirazin- 2- ilamina	1.15	ver ejemplo	(300 MHz, $CDCl_3$) δ 2.72 (m, 4H), 3.80 (s, 6H), 4.73 (s, 2H), 5.73 (s, 2H), 7.06 (m, 1H), 7.20 (m, 1H), 7.46 (d, 1H), 7.80 (dd, 1H), 8.12 (s, 1H), 8.25 (s, 1H)	486
II- 69		3- [1- (2- cloro- 3,6- difluoro- fenil)- 2- metil- propoxi]- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- pirazin- 2- ilamina	10.58	ver ejemplo	(400 MHz, DMSO- d_6) δ 0.89 (d, 3H), 1.19 (d, 3H), 2.47 (m, 4H), 2.56 (m, 1H), 2.68 (t, 2H), 3.56 (t, 4H),4.07 (t, 2H), 5.96 (d, 1H), 6.28 (s, 2H), 6.89 (d, 2H), 7.26 (m, 1H), 7.38 (m, 1H), 7.63 (d, 2H), 7.95 (m, 1H)	519
II- 70	 TFA	3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- pirazin- 2- ilamina; compuesto con acido trifluoro- acetico	0.51	ver ejemplo	(400 MHz, DMSO- d_6) δ 1.78 (d, 3H), 3.21 (m, 2H), 3.51 (m, 2H), 3.54 (m, 2H), 3.98 (m, 2H), 4.38 (t, 2H), 6.34 (br s, 2H), 6.45 (m, 1H), 6.97 (d, 2H), 7.25 (m, 1H), 7.38 (m, 1H), 7.66 (d, 2H), 7.86 (s, 1H)	491

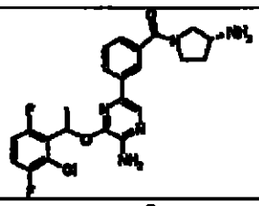
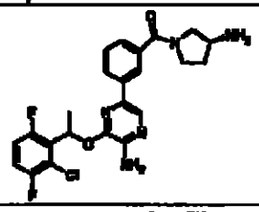
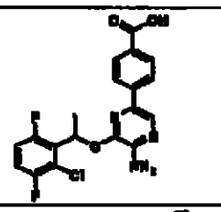
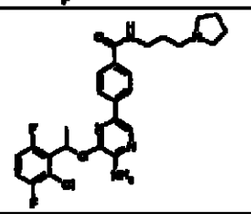
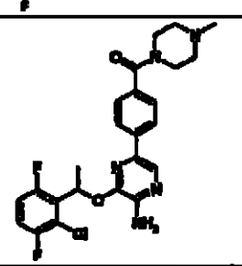
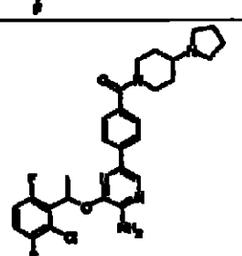
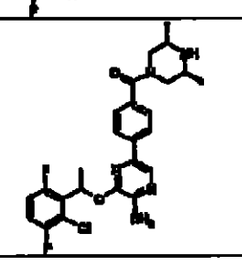
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 71	 TFA	3- [1- (2,6- dicloro- 3,6- fluoro- fenil)- etoxi]- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- pirazin- 2- ilamina; compuesto con acido trifluoro- acetico	0.3	ver ejemplo	(400 MHz, DMSO- d_6) δ 1.79 (d, 3H), 3.21 (m, 2H), 3.46 (m, 2H), 3.57 (m, 2H), 3.74 (m, 2H), 3.95 (m, 2H), 4.36 (t, 2H), 6.34 (br s, 2H) 6.49 (m, 2H), 6.94 (m, 1H), 7.37 (t, 1H), 7.48 (m, 1H), 7.66 (d, 2H), 7.98 (s, 1H)	491
II- 72		N- (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- metanesulfonamida		ver ejemplo	(400 MHz, DMSO- d_6) δ 1.78 (d, 3H), 2.96 (s, 3H), 6.41 (m, 3H), 7.15(d, 2H), 7.26 (m, 1H), 7.37 (m, 1H), 7.64 (d, 2H), 8.00 (s, 1H), 9.72 (s, 1H)	455
II- 73		ácido 2- pirrolidin- 1- il- etanosulfonico (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}fenil)- amida		ver ejemplo	(300 MHz, $CDCl_3$) δ 1.84 (m, 7H), 2.56 (m, 4H), 3.04 (m, 2H), 3.25 (m, 2H), 4.91 (br s, 2H), 6.71 (q, 1H), 6.95 (m, 2H), 7.21 (d, 2H), 7.72 (d, 2H), 7.96 (s, 1H)	538
II- 74		ácido 2- (4- hidroxi- piperidin- 1- il- etanosulfonico (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}fenil)- amida		ver ejemplo	(300 MHz, $CDCl_3$) δ 1.60 (m, 2H), 1.82 (m, 5H), 2.32 (m, 2H), 2.77 (m, 2H), 2.89 (t, 2H), 3.26 (t, 2H), 3.74 (m, 1H), 5.07 (br s, 2H), 6.70 (q, 1H), 7.00 (m, 2H), 7.24 (d, 2H), 7.73 (d, 2H), 7.94 (s, 1H)	568
II- 75		acido piperidin- 1- il- etanosulfonico (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}fenil)- amida		ver ejemplo	(300 MHz, $CDCl_3$) δ 1.49 (m, 2H), 1.61 (m, 4H), 1.83 (d, 3H), 2.50 (m, 4H), 2.86 (m, 2H), 3.20 (m, 2H), 4.95 (br s, 2H), 6.70 (q, 1H), 7.00 (m, 2H), 7.24 (d, 2H), 7.74 (d, 2H), 7.96 (s, 1H)	552
II- 76		acido 2- (ciclopropilmetil- amino)- etanosulfonico (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}fenil)- amida		ver ejemplo	(300 MHz, $CDCl_3$) δ 0.14 (m, 2H), 0.50 (m, 2H), 0.95 (m, 1H), 1.82 (d, 3H),2.49 (m, 2H), 3.20 (m, 4H), 4.73 (br s, 1H), 5.02 (br s, 2H), 6.71 (q, 1H), 7.00 (m, 2H), 7.25 (d, 2H), 7.74 (d, 2H), 7.96 (s, 1H)	538
II- 77		acido 2 - [(3R)- 3- hidroxi- pirrolidin- 1- il]- etanosulfonico (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida		ver ejemplo	(300 MHz, $CDCl_3$) δ 1.79 (m, 1H), 1.82 (d, 3H), 2.26 (m, 2H), 2.54 (m, 1H), 2.82 (m, 1H), 3.08 (m, 1H), 3.26 (m, 2H),4.44 (m, 1H), 4.94 (br s, 1H), 6.70 (q, 1H), 7.00 (m, 2H), 7.29 (d, 2H), 7.73 (d, 2H), 7.96 (s, 1H)	554

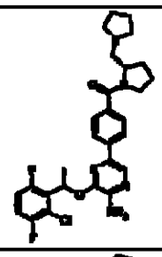
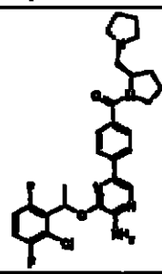
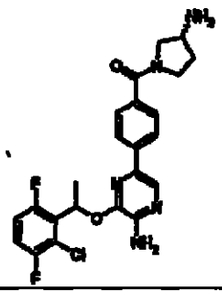
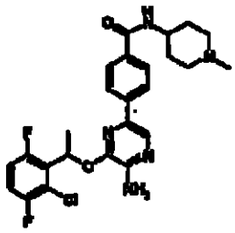
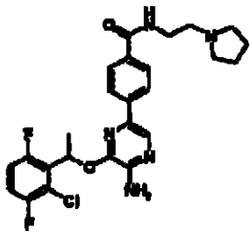
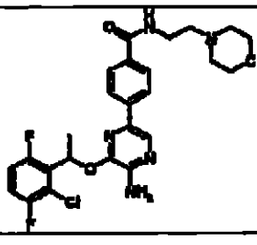
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 78		acido 2- [(2S)- 2- hidroximetil- pirrolidin- 1- il]- etanosulfonico (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida		ver ejemplo	(300 MHz, $CDCl_3$) δ 1.79 (m, 4H), 1.82 (d, 3H), 2.15 (m, 1H), 2.66 (m, 2H), 2.98 (m2, H), 3.35 (m, 1H), 3.8 (m, 1H), 3.54 (m, 1H), 3.92 (m, 1H), 4.97 (br s, 1H), 6.71 (q, 1H),7.00 (m, 2H), 7.28 (d, 2H), 7.71 (d, 2H), 7.95 (s, 1H)	568
II- 79		acido 2- dimetilamino- etanosulfonico (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida		ver ejemplo	(300 MHz, $CDCl_3$) δ 1.82 (d, 3H), 2.29 (s, 6H), 2.85 (t, 2H), 3.21 (t, 2H), 5.00 (br s, 2H), 6.71 (q, 1H) 7.00 (m, 2H), 7.23 (d, 2H), 7.74 (d, 2H), 7.96 (s, 1H)	512
II- 80		acido 2- morfolin- 4- il- etanosulfonico (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida		ver ejemplo	(300 MHz, $CDCl_3$) δ 1.82 (d, 3H), 2.48 (m, 4H), 2.90 (m, 2H), 3.27 (m, 2H), 3.71 (m, 4H), 4.92 (br s, 2H), 6.71 (q, 1H), 7.00 (m, 2H), 7.24 (d, 2H), 7.74 (d, 2H), 7.97 (s, 1H)	554
II- 81		acido 2-dietilamino- etanosulfonico (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida		ver ejemplo	(300 MHz, $CDCl_3$) δ 1.07 (t, 6H), 1.82 (d, 3H), 2.60 (q, 4H), 3.02 (t, 2H), 3.22 (t, 2H), 4.95 (br s, 2H), 6.71 (q, 1H), 7.00 (m, 2H), 7.22 (d, 2H), 7.74 (d, 2H), 7.96 (s, 1H)	540
II- 82		acido 2 ciclopropilamino- etanosulfonico (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida		ver ejemplo	(300 MHz, $CDCl_3$) δ 0.38 (m, 2H), 0.50 (m, 2H), 1.82 (d, H), 2.15 (m, 1H), 3.24 (m, 4H), 4.95 (br s, 2H), 6.71 (q, 1H), 7.00 (m, 2H), 7.21 (d, 2H). 7.74 (d, 2H), 7.97 (s, 1H)	540
II- 83		3- [5-amino- 6[1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- acido benzoico	1.36	ver ejemplo		423
II- 84		(3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- [(3S)- 3- amino- pirrolidin- 1- il)- metanona	0.069	ver ejemplo	(300 MHz, MeOD) δ 7.84 (d, 1H), 7.71 (m, 2H), 7.38 (m, 3H), 7.10 (m, 1H), 6.60 (m, 1H), 4.86 (s, 2H), 4.20 (m, 1H), 3.45- 3.89 (m, 4H), 1.82 (d, 3H), 1.34 (m, 1H), 0.89 (m, 1H)	492

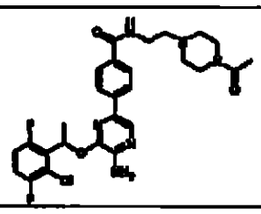
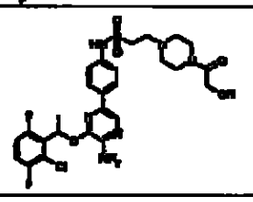
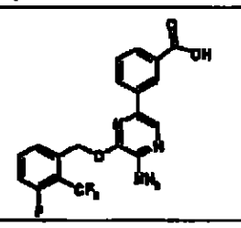
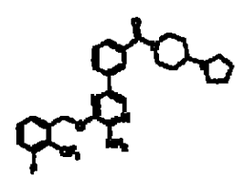
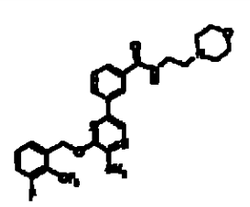
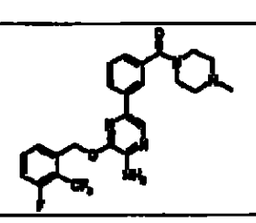
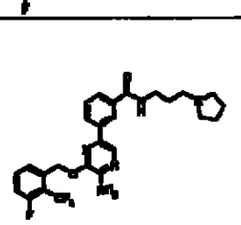
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 85		(3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- [(3R)- 3- amino- pirrolidin- 1- il)- metanona	0.11	ver ejemplo	(300 MHz, MeOD) δ 7.84 (d, 1H), 7.71 (m, 2H), 7.38 (m, 3H), 7.10 (m, 1H), 6.60 (m, 1H), 4.86 (s, 2H), 4.20 (t, 1H), 3.45- 3.89 (m, 4H), 1.82 (d, 3H), 1.34 (m, 1H), 0.89 (m, 1H)	492
II- 86		(3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.15	ver ejemplo	(300 MHz, $CDCl_3$) δ 8.04 (d, 1H), 7.84 (d, 2H), 7.30 (d, 2H), 7.1 (tert, 1H), 6.99 (t, 1H), 5.89 (m, 1H), 4.89 (s, 2H), 4.44 (s, 1H), 3.89 (m, 1H), 3.65 (m, 1H), 3.30 (m, 2H), 2.85 (m, 3H), 1.82 (d, 3H), 0.89- 2.20 (m, 9H)	558
II- 87		N- [2- (4- Acetil- piperazin- 1- il)- etil]- 3- (5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il)- benzamida	0.186	ver ejemplo	(300 MHz, $CDCl_3$) δ 8.04 (d, 1H), 7.99 (s, 1H), 7.78 (d, 1H), 7.60 (d, 1H), 7.34 (m, 2H), 7.15 (t, 1H), 6.72 (tert, 1H), 4.89 (s, 2H), 4.56 (m, 6H), 3.21 (d, 3H), 2.60 (t, 1H), 2.55 (dd, 1H), 2.09 (s, 3H), 1.80 (d, 4H)	575
II- 88		(3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)-metanona	0.17	ver ejemplo	(300 MHz, MeOD) δ 8.04 (d, 1H), 7.84 (d, 2H), 7.35 (m, 3H), 7.20 (m, 1H), 6.60 (m, 1H), 4.89 (s, 2H), 4.44 (s, 1H), 3.59 (m, 1H), 3.30 (m, 1H), 3.25 (s, 2H), 3.16 (m, 3H), 1.82 (d, 3H), 0.89- 2.32 (m,9H)	559
II- 89		acido 3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- benzoico		ver ejemplo		406
II- 90		3- {5- amino- 6- [1- (2- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4- il)- benzamida	0.21	ver ejemplo	(300 MHz, $CDCl_3$) δ 8.20 (s, 1H), 8.08 (s, 1H), 7.89 (d, 1H), 7.75 (d, 1H), 7.44 (t, 1H), 7.01 (m, 2H), 6.78 (m, 1H), 6.20 (s, 1H), 4.98 (s, 2H), 4.09(m, 1H), 2.97(m, 2H), 2.39 (s, 3H), 2.29 (t, 2H), 2.12 (m, 2H), 1.90 (d,3 H), 1.79 (m, 2H)	502
II- 91		3- {5- amino- 6- [1- (2- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- il- pirrolidin- 1- il- propil)- benzamida	0.15	ver ejemplo	(300 MHz, CD_3OD) δ 8.15 (s, 1H),7.98 (s, 1H) 7.80 (d, 1H), 7.61 (d, 1H), 7.35 (m, 2H), 7.09 (t, 1H), 6.69 (m, 1H), 3.44 (t, 2H), 2.55 (m, 6H), 1.88 (d, 3H), 1.80 (m, 6H)	532

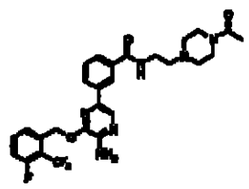
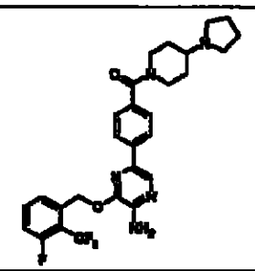
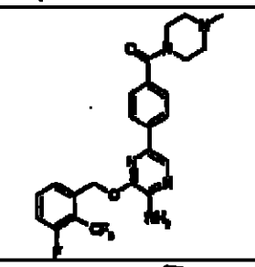
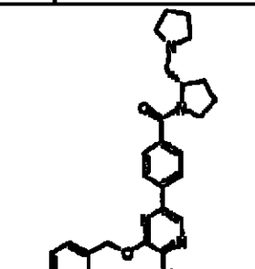
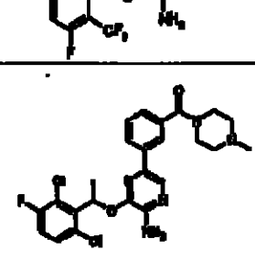
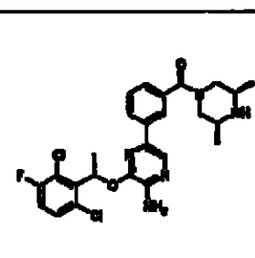
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 92		(3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	0.15	ver ejemplo	(300 MHz, CD- $_3$OD) δ 7.96 (s, 1H), 7.76 (d, 1H), 7.65 (m, 1H), 7.41 (m, 2H), 7.21 (d, 1H), 7.12 (t, 1H), 6.61 (m, 1H), 4.68 (m, 2H), 3.62 (m, 1H), 3.05 (m, 2H), 2.69 (m, 6H), 2.45 (m, 2H), 2.12 (m, 2H), 1.86 (d, 3H), 1.48 (m, 2H)	558
II- 93		acido 4- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi- - pirazin- 2- il]- benzoico		ver ejemplo		408
II- 94		4- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi- - pirazin- 2- il]- N- (2- morfolin- 4- il- etil)- benzamida	0.22	ver ejemplo	(300 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.92 (d, 2H), 7.84 (d, 2H), 7.50 (m, 1H), 7.42 (m, 1H), 7.20 (m, 1H), 6.75 (s, 1H), 5.70 (s, 2H), 4.97 (s, 2H), 3.74 (m, 4H), 3.58 (m, 2H), 2.62 (m, 2H), 2.52 (s, 4H)	520
II- 95		4- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi- - pirazin- 2- il]- N- (1- metil- piperidin- 4- il)- benzamida	0.081	ver ejemplo	(300 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.92 (d, 2H), 7.84 (d, 2H), 7.50 (m, 1H), 7.42 (m, 1H), 7.20 (m, 1H), 6.04 (d, 1H), 5.75 (s, 2H), 5.01 (s, 2H), 4.0 (m, 1H), 2.85 (d, 2H), 2.30 (s, 3H), 2.20 (t, 2H), 2.12 (d, 2H), 1.59 (m, 2H)	504
II- 96		3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- pirrolidin- 1- il- propil)- benzamida	0.15	4 como en el ejemplo II 84	(300 MHz, CD3OD) δ 8.18 (s, 1H), 7.98 (s, 1H), 7.80 (d, 1H), 7.61 (d, 1H), 7.35 (m, 2H), 7.12 (t, 1H), 6.75 (q, 1H), 3.44 (t, 2H), 2.55 (m, 6H), 1.88 (d, 3H), 1.80 (m, 6H).	532
II- 97		3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)etoxi]- pirazin- 2- il}- N- (3- pirrolidin- 1- il- propil)- benzamida	035	4 como en el ejemplo II 84	(300 MHz, $CDCl_3$) δ 8.38 (s.1H), 8.18 (s, 2H), 7.92 (m, 2H), 7.48 (t. 1H) 7.02 (m, 2H) 6.78 (q, 1H), 4.96 (s, 2H), 3.72 (m, 2H), 3.18 (m, 2H), 2.83 (m, 2H), 2.22 (m, 2H), 2.08 (m, 4H), 1.83 (d, 3H) 1.70 (m, 2H).	516
II- 98		3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)etoxi]- pirazin- 2- il}- N- (1- metil- piridin- 4- il)- benzamida	0.21	4 como en el ejemplo II 84	(300 MHz, $CDCl_3$) δ 8.20 (s, 1H), 8.08 (s, 1H), 7.89 (d, 1H), 7.75 (d, 1H), 7.44 (t, 1H) 7.01 (m, 2H), 6.78 (q, 1H), 6.20 (bd, 1H), 4.98 (s, 2H), 4.09 (m, 1H), 2.97 (m, 2H), 2.39 (s, 3H), 2.29 (m, 2H), 2.12 (m, 2H), 1.90 (d, 3H), 1.79 (m, 2H).	502

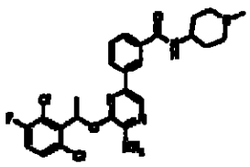
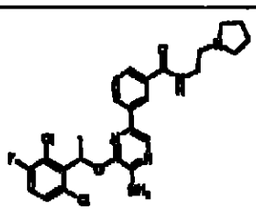
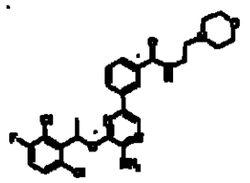
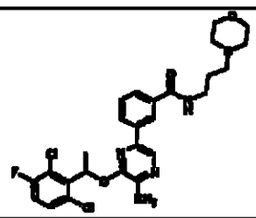
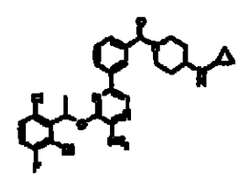
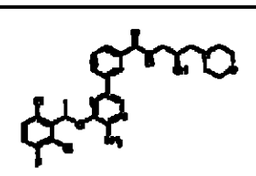
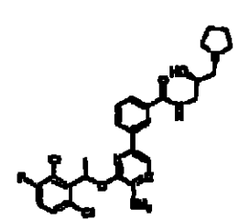
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^1H- NMR	MS m/z (M+1)
II- 99		3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)etoxi]- pirazin- 2- il}- N- (2- pirrolidin- 1- il- etil)- benzamida	0.18	4 como en el ejemplo II 84	(300 MHz, $CDCl_3$) δ 8.19 (s, 1H), 8.09 (s, 1H), 7.88 (d, 1H), 7.78 (d, 1H), 7.48 (t, 1H), 7.06 (bm, 1H), 6.96 (m, 2H), 6.75 (q, 1H), 5.08 (s, 2H), 3.68 (m, 2H), 2.88 (m, 2H), 2.68 (m, 4H),1.86 (m, 7H).	502
II- 100		3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- benzamida	0.31	4 como en el ejemplo II 84	(300 MHz, $CDCl_3$) δ 8.17 (s, 1H), 8.08 (s, 1H), 7.88 (d, 1H) 7.68 (d 1H), 7.48 (t, 1H), 6.98 (m, 2H), 6.80 (bt, 1H), 6.74 (q, 1H), 5.02 (s, 2H), 3.76 (m, 4H), 3.68 (m, 2H), 2.68 (m, 2H), 2.58 (m, 4H), 1.85 (d, 3H).	518
II- 101		N- [2- (4- acetil- piperazin- 1- il)- etil]- 3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- benzamida	0.64	4 como en el ejemplo II 84	(300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 8.03 (s, 1H), 7.86 (d, 1H), 7.68 (d, 1H), 7.40 (t, 1H), 6.98 (m, 3H), 6.71 (q, 1H), 5.13 (s, 2H), 3.69 (m, 4H), 3.51 (m, 2H), 2.80 (m, 2H), 2.66 (m, 4H), 2.08 (s, 3H), 1.83 (d, 3H).	559
II- 102		(3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- metil piperazin- 1- il)- metanona		4 como en el ejemplo II 84	(300 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.82 (m, 2H), 7.41 (t, 1H), 7.28 (m, 1H), 6.95 (m, 2H), 6.71 (q, 1H), 5.00 (s, 2H), 3.85 (m, 2H), 3.46 (m, 2H), 2.36 (m, 4H), 2.33 (s, 3H), 1.63 (d, 3H).	488
II- 103		(3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona		4 como en el ejemplo II 84	(300 MHz, $CDCl_3$) δ 8.02 (s. 1H), 7.80 (m, 2H), 7.41 (t, 1H) 7.29 (m, 1H), 6.95 (m, 2H), 6.69 (q, 1H), 4.97 (s, 2H), 4.72 (m, 1H), 3.83 (m, 1H), 2.81 (m, 7H), 1.83 (d, 3H), 2.10- 1.70 (m, 8H).	542
II- 104		(3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((3R- 5S)- 3,5- dimetil- piperazin- 1- il)- metanona		4 como en el ejemplo II 84	(300 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.80 (m, 2H), 7.41 (t, 1H), 7.29 (m, 1H), 6.95 (m, 2H), 6.70 (q, 1H), 5.00 (s, 2H), 4.68 (m, 1H), 3.56 (m, 1H), 2.75 (m, 3H), 2.42 (m, 1H), 1.83 (d, 3H), 1.57(m, 1H), 1.15 (m, 3H), 0.96 (m, 3H).	502
II- 105		(3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona		4 como en el ejemplo II 84	(300 MHz, $CDCl_3$) δ 8.04 (s. 1H), 7.83 (m, 2H), 7.39 (m, 2H), 6.98 (m, 2H), 6.70 (q, 1H). 5.00 (s, 2H), 4.47 (m, 1H), 3.50 (m, 2H), 3.00 (m, 5H), 2.30 (m, 3H), 2.00 (m, 5H), 1.83 (d, 3H), 1.53 (m, 1H).	542

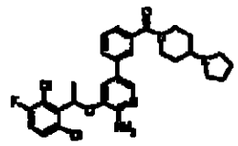
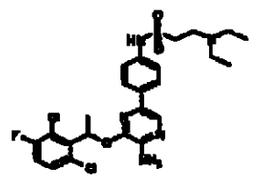
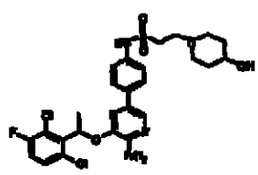
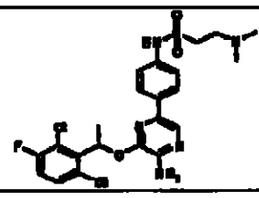
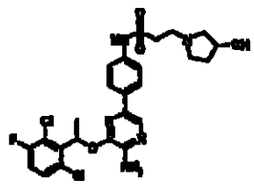
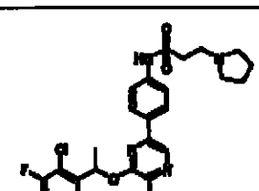
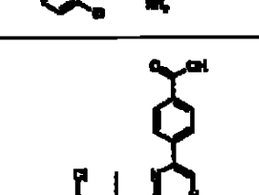
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 106		(3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona		4 como en el ejemplo II 84	(300 MHz, $CDCl_3$) δ 8.02(s, 1H), 7.83 (m, 2H), 7.40 (m, 2H), 6.98 (m, 2H), 6.70 (q, 1H), 4.98 (s, 2H), 3.75 (m, 4H), 3.61- 3.15 (m, 1H), 2.15 (m, 1H), 1.85 (d, 3H), 1.95- 1.75 (m, 3H).	300
II- 107		(3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((S)- 3- amino- pirrolidin- 1- il)- metanona		4 como en el ejemplo II 84	(300 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.83 (m, 2H), 7.40 (m, 2H), 6.98 (m, 2H), 6.70 (q, 1H), 4.98 (s, 2H), 3.75 (m, 4H), 3.61- 3.15 (m, 1H), 2.15 (m, 1H), 1.85 (d, 3H), 1.95- 1.75 (m, 3H).	300
II- 108		4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona		3 como en el ejemplo I- 211		406
II- 109		4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- pirrolidin- 1- il- propil)- benzamida	0.1	4 como en el ejemplo II109	(300 MHz, $CDCl_3$) δ 5.28 (bm, 1H), 8.04 (m, 3H), 7.84 (d, 2H), 6.95 (m, 2H), 6.71 (q, 1H), 5.03 (s, 2H), 3.85 (m, 2H), 3.72 (m, 2H), 3.18 (m, 2H), 2.82 (m, 2H), 2.25 (m, 4H), 2.08 (m, 2H), 1.87 (d, 3H).	516
II- 110		4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- metil- piperazin- 1- il)- metanona	0.16	4 como en el ejemplo II109	(300 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.78 (d, 2H), 7.43 (d, 2H), 7.29 (m, 1H), 6.85 (t, 1H), 6.94 (q, 1H), 5.07 (s, 2H), 3.75 (m, 2H), 3.50 (m, 2H), 2.43 (m, 4H), 2.33 (s, 3H), 1.84 (d, 3H).	488
II- 111		4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- pirrolidin- 1- il- piperin- 1- il)- metanona	0.17	4 como en el ejemplo II109	(300 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.81 (d, 2H), 7.40 (d, 2H), 6.99 (m, 2H), 6.71 (q, 1H), 5.02 (s, 2H), 4.64 (m, 1H), 3.85 (m, 1H), 2.99 (m, 2H), 2.67 (m, 4H), 2.38 (m, 1H), 1.80 (m, 9H), 1.62 (m, 2H).	542
II- 112		4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((3R- 5S)- 3,5- dimetil- piperazin- 1- il)- metanona	0.19	4 como en el ejemplo II109	(300 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.81 (d, 2H), 7.38 (d, 2H), 6.99 (m, 2H), 6.71 (q, 1H), 4.99 (s, 2H), 4.65 (m, 1H), 3.65 (m, 1H), 2.88 (m, 2H), 2.68 (m, 1H), 2.41 (m, 1H), 1.84 (d, 3H), 1.64 (m, 1H), 1.18 (s, 3H), 1.06 (s, 3H).	502

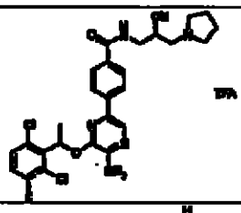
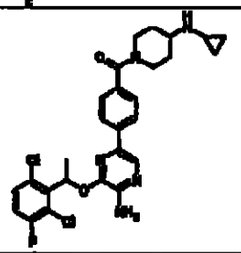
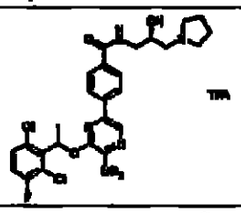
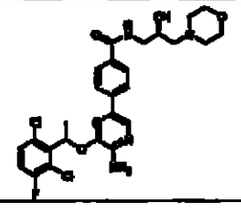
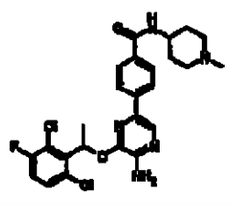
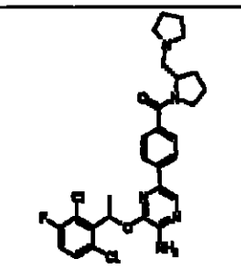
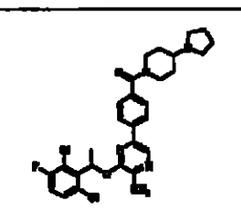
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 113		(4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.18	4 como en el ejemplo II109	(300 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.81 (d, 2H), 7.53 (d, 2H), 6.95 (m, 2H), 6.69 (q, 1H), 4.99 (s, 2H), 4.45 (m, 1H), 3.55 (m, 2H), 2.95 (m, 4H), 1.90- 2.3 (m, 9H), 1.82 (d, 3H), 1.65 (m, 1H).	542
II- 114		(4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.13	4 como en el ejemplo II109	(300 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.81 (d, 2H), 7.53 (d, 2H), 6.95 (m, 2H), 6.69 (q, 1H), 4.99 (s, 2H), 4.45 (m, 1H), 3.55 (m, 2H), 2.95 (m, 4H), 2.21 (m, 3H), 1.92 (m, 6H), 1.82 (d, 3H), 1.59 (m, 1H).	542
II- 115		4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona	0.078	4 como en el ejemplo II109	(300 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.81 (d, 2H), 7.53 (d, 2H), 7.01 (m, 2H), 6.69 (q, 1H), 4.91 (s, 2H), 3.85 (m, 1H), 3.71 (m, 2H), 3.55 (m, 1H), 2.18 (m, 1H), 1.85 (d, 3H), 1.75 (m, 1H), 1.42 (m, 3H).	574
II- 116		4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4- il)- benzamida	0.19	4 como en el ejemplo II109	(300 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.82 (m, 4H), 7.00 (m, 2H), 6.72 (m, 2H), 5.04 (s 2H), 4.09 (m, 1H), 2.97 (m, 2H), 2.39 (s, 3H), 2.29 (m, 2H), 2.12 (m, 2H), 1.90 (d, 3H), 1.79 (m, 2H).	502
II- 117		4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- pirrolidin- 1- il- etil)- benzamida	0.11	4 como en el ejemplo II109	(300 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.82 (m, 4H), 7.00 (m, 2H), 6.72 (m, 2H), 5.04 (s, 2H), 3.68 (m, 2H), 2.88 (m, 2H), 2.68 (m, 4H), 1.86 (m, 7H).	502
II- 118		4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- benzamida	0.26	4 como en el ejemplo II109	(300 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.82 (m, 4H), 7.00 (m, 2H), 6.72 (m, 2H), 5.04 (s, 2H), 3.75 (m, 4H), 3.56 (m, 2H), 2.62 (t, 2H), 2.52 (m, 4H), 1.83 (d, 3H).	518

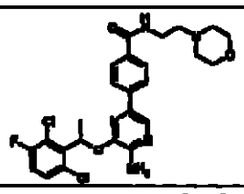
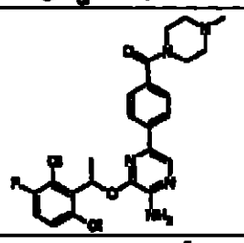
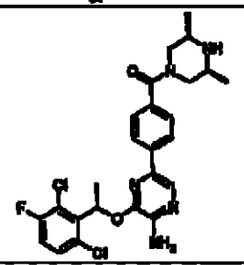
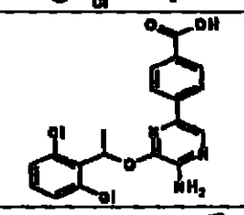
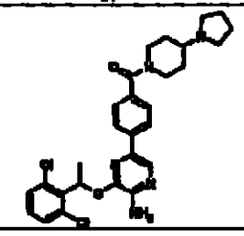
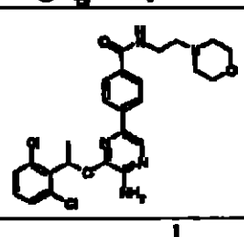
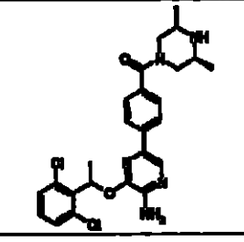
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 119		N- [2- (4- acetil- piperazin- 1- il)- etil]- 4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- benzamida	0.48	4 como en el ejemplo II109	(300 MHz, $CDCl_3$) δ 8.08 (s, 1 H), 7.82 (m, 4H), 7.00 (m, 2H), 6.70 (m, 2H), 5.03 (s, 2H), 3.62 (m, 4H), 3.50 (m, 2H), 2.65 (t, 2H), 2.52 (m, 4H), 2.10 (s, 3H), 1.83 (d, 3H).	559
II- 120		ácido 2- [4- (2- hidroxi- acetil)- piperazin- 1- il]- etanosulfónico (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida	0.19	3 como en el ejemplo I- 243	(300 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.75 (d, 2H), 7.24 (m, 3H), 7.08 (m, 1H), 6.95 (m, 1H), 6.70 (q, 1H), 5.02 (s, 2H), 4.14 (s, 2H), 3.64 (m, 3H), 3.25 (m, 4H), 2.91 (m, 2H), 2.44 (m, 4H), 1.83 (d, 3H).	611
II- 121		ácido 3- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- benzoico		3 como en el ejemplo I- 211		408
II- 122		3- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	0.19	4 como en el ejemplo II- 122	(300 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.88 (m, 2H), 7.56 (m, 1H), 7.44 (t, 1H), 7.34 (d, 1H), 7.21 (t, 1H), 5.69 (s, 2H), 4.92 (s, 2H), 4.70 (m, 1H), 3.82 (m, 1H), 3.06 (m, 1H), 2.98 (m, 1H), 2.65 (m, 4H), 2.28 (m, 1H), 1.02 (m, 1H), 1.81 (m, 5H), 1.55 (m, 2H).	544
II- 123		3- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- N- {2- [etil- (2- metoxi- etil)- amino]- etil}- benzamida	0.45	4 como en el ejemplo II- 122	(300 MHz, $CDCl_3$) δ 8.34 (s, 1H), 8.14 (s, 1H), 8.01 (d, 1H), 7.68 (d, 1H), 7.53 (m, 1H), 7.50 (t, 1H), 7.45 (d, 1H), 7.21 (t, 1H), 6.79 (bm, 1H), 5.72 (s, 2H), 4.92 (s, 2H), 3.72 (m, 4H), 3.61 (m, 2H), 2.66 (m, 2H), 2.55 (m, 4H).	520
II- 124		{3- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- fenil}- (4- metil- piperazin- 1- il)- metanona	0.23	4 como en el ejemplo II- 122	(300 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.90(m, 2H), 7.60- 7.20 (m, 5H), 5.70 (s, 2H), 4.91 (s, 2H), 3.85 (m, 2H), 3.50 (m, 2H), 2.52 (m, 2H), 2.32 (m, 2H), 2.33 (s, 3H).	490
II- 125		3- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- N- {3- pirrolidin- 1- il- propil}- benzamida	0.22	4 como en el ejemplo II- 122	(300 MHz, $CDCl_3$) δ 8.85 (bm, 1H), 8.34 (s, 1H), 8.13 (s, 1H), 7.95 (d, 1H), 7.60 (d, 1H), 7.56 (m, 1H), 7.45 (m, 2H), 7.20 (t, 1H), 5.72 (s, 2H), 4.92 (s, 2H), 3.61 (m, 2H), 2.72 (m, 2H), 2.57 (m, 4H), 1.82 (m, 2H), 1.76 (m, 4H).	518

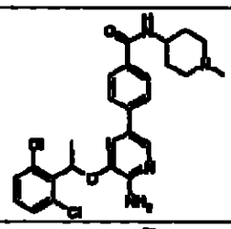
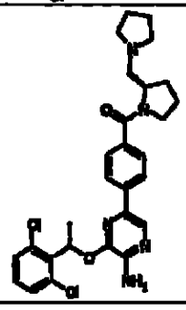
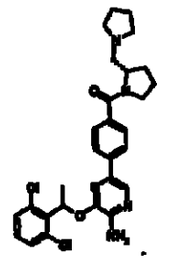
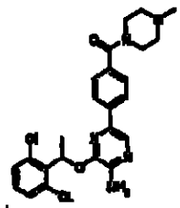
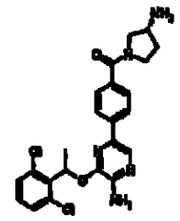
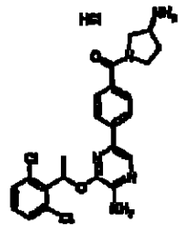
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 126		N- [2- (4- acetil- piperazin- 1- il)- etil]- 3- [5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- benzamida	0.65	4 como en el ejemplo II- 122	(300 MHz, $CDCl_3$) δ 8.28 (s, 1H), 8.14 (s, 1H), 7.99 (d, 1H), 7.67 (d, 1H), 7.58 (m, 1H), 7.52 (t, 1H), 7.42 (d, 1H), 7.22 (t, 1H), 6.75 (bm, 1H), 5.72 (s, 2H), 4.95 (s, 2H), 3.62 (m, 4H), 3.47 (m, 2H), 2.63 (m, 2H), 2.52 (m, 4H), 2.08 (s,3H).	561
II- 127		{4- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	0.047	4 como en el ejemplo II- 94	(300 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.88 (d, 2H), 1H), 7.52 (m, 1H), 7.44 (d, 2H), 7.42 (m, 1H), 7.20 (t, 1H), 5.71 (s, 2H), 5.05 (s, 2H), 4.62 (m, 1H), 3.82 (m, 1H), 3.06 (m, 1H), 2.98 (m, 1H), 2.65 (m, 4H), 2.28 (m, 1H), 1.02 (m, 1H), 1.81 (m, 5H), 1.55 (m, 2H).	544
II- 128		{4- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- fenil}- (4- metil- piperazin- 1- il)- metanona	0.15	4 como en el ejemplo II- 94	(300 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.88 (d, 2H), 7.55- 7.40 (m, 4H), 7.21 (t, 1H), 5.72 s, 2H), 5.01 (s, 2H), 3.82 (m, 2H), 3.50 (m, 2H), 2.50 (m, 2H), 2.32 (m, 2H), 2.33 (s, 3H).	490
II- 129		{4- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- fenil}- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.052	4 como en el ejemplo II- 94	(300 MHz, $CDCl_3$) δ 8.11 (s. 1H), 7.88 (d, 2H),7.68 (m, 3H), 7.42 (d, 1H), 7.22 (t, 1H), 5.72 (m, 2H), 4.92 (s, 2H), 3.50 (m, 2H), 3.74 (m, 4H), 1.84 (d, 3H), 1.57- 2.18 (m, 11H).	544
II- 130		(3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- metil- piperazin- 1- il)- metanona	0.17	4 como en el ejemplo II- 84	(300 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.79 (m, 2H), 7.40 (t, 1H), 7.29 (m, 1H), 7.01 (t, 1H), 6.81 (q, 1H), 5.06 (s, 2H), 3.85 (m, 2H), 3.46 (m, 2H), 2.51 (m, 2H), 2.35 (m, 2H), 2.33 (s, 3H), 1.84 (d, 3H).	506
II- 131		(3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((3R, 5R)- 3,5- dimetil- piperazin- 1- il)- metanona	0.12	4 como en el ejemplo II- 84	(300 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.78 (m, 2H), 7.39 (t, 1H), 7.24 (m, 1H), 7.01 (t, 1H), 6.81 (q, 1H), 5.07 (s, 2H), 4.71 (m, 1H), 3.58 (m, 1H), 2.96 (m, 1H), 2.82 (m, 1H), 2.66 (m, 1H), 2.42 (m, 1H), 1.84 (d, 3H), 1.74 (m, 1H), 1.22 (d, 3H), 1.00 (d, 3H).	518

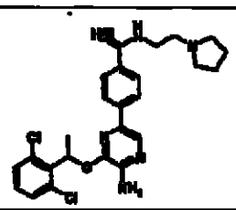
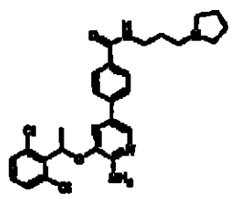
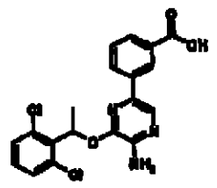
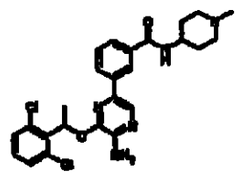
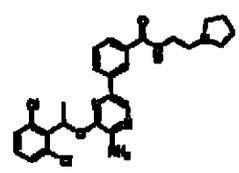
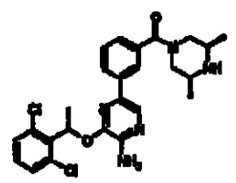
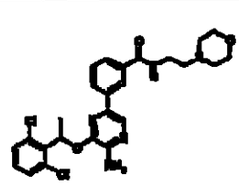
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 132		3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4- il)- benzamida	0.13	4 como en el ejemplo II- 84	(300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.99 (s, 1H),7.82 (d, 1H), 7.66 (d, 1H), 7.42 (m, 2H), 7.15 (t, 1H), 6.74 (q, 1H), 3.95 (m, 1H), 2.98 (m, 2H), 2.34 (s, 3H), 2.25 (m, 2H), 2.01 (m, 2H), 1.84 (d, 3H), 1.73 (m, 2H).	520
II- 133		3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- pirrolidin- 1- il- etil)- benzamida	0.17	4 como en el ejemplo II- 84	(300 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.99 (s, 1H), 7.82 (d, 1H), 7.66 (d, 1H), 7.38 (m, 2H) 7.12 (t, 1H), 6.72 (q, 1H), 3.64 (m, 2H), 2.86 (m, 2H), 2.75 (m, 4H), 2.25 (m, 2H), 2.01 (m, 2H), 1.84 (m, 7H).	520
II- 134		3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- benzamida	0.21	4 como en el ejemplo II- 84	(300 MHz, $CDCl_3$) δ 8.13 (s, 1H), 8.03 (s, 1H), 7.85 (d, 1H), 7.67 (d, 1H), 7.42 (t, 1H), 7.28 (dd,1H), 7.00 (t, 1H), 6.86 (q, 1H), 6.84 (bm, 1H), 5.11 (s, 2H), 3.72 (m, 4H), 3.61 (m, 2H), 2.63 (m, 2H), 2.53 (m, 4H), 1.84 (d, 3H).	534
II- 135		3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- morfolin- 4- il- propil)- benzamida	0.26	4 como en el ejemplo II- 84	(300 MHz, $CDCl_3$) δ 8.19 (s, 1H), 8.06 (s, 1H), 7.87 (d, 1H), 7.70 (bm, 1H), 7.67 (d, 1H), 7.42 (t, 1H), 7.28 (dd, 1H), 7.01 (t, 1H), 6.86 (q, 1H), 5.11 (s, 2H), 3.64 (m, 6H), 2.54 (m, 2H), 2.48 (m, 4H), 1.84 (m, 5H).	548
II- 136		(3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- ciclopropilamino- piperidin- 1- il)- metanona	0.15	4 como en el ejemplo II- 84		544
II- 137		3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- ((S)- 2- hidroxi- 3- morfolin- 4- il- propil)- benzamida	0.3	4 como en el ejemplo II- 84		564
II- 138		3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- ((R)- 2- hidroxi- 3- pirrolidin- 1- il- propil)- benzamida	0.13	4 como en el ejemplo II- 84		548

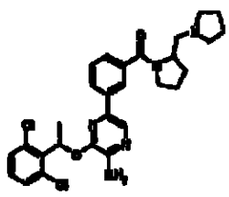
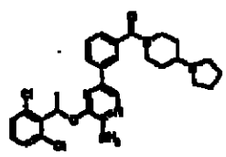
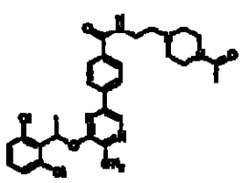
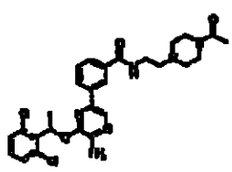
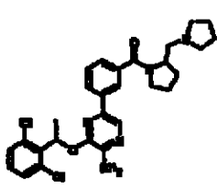
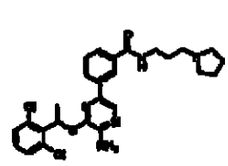
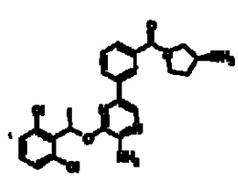
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H-NMR	MS m/z (M+1)
II-139		(3-{6-amino-5-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-piridin-3-il}-fenil)-(4-pirrolidin-1-il-piperidin-1-il)-metanona	0.071	4 como en el ejemplo II-84	(300 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.41 (m, 3H), 7.30 (m, 3H), 7.07 (t, 1H), 6.99 (s, 1H), 6.12 (q, 1H), 4.95 (s, 2H), 4.70 (m, 1H), 3.82 (m, 1H), 3.06 (m, 1H), 2.98 (m, 1H), 2.65 (m, 4H), 2.28 (m, 1H), 1.02 (m, 1H), 1.81 (m, 5H), 1.55 (m, 2H).	559
II-140		ácido 2-dietilamino-etanosulfonico (4-{5-amino-6-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-pirazin-2-il}-fenil)-amida	0.35	3 como en el ejemplo I-243	(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.70 (d, 2H),7.28 (m, 2H), 7.21 (d, 2H), 7.01 (t, 1H), 6.82 (q, 1H), 5.05 (s, 2H), 3.22 (m, 2H), 3.00 (m, 2H), 2.55 (m, 4H), 1.83 (d, 3H), 1.60 (d, 6H),	556
II-141		ácido 2-(4-hidroxi-piperidin-1-il)-etanosulfonico (4-{5-amino-6-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-pirazin-2-il}-fenil)-amida	0.21	3 como en el ejemplo I-243	(300 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.71 (d, 2H), 7.28 (m, 2H), 7.21 (d, 2H), 7.01 (t, 1H), 6.82 (q, 1H), 5.00 (s, 2H), 3.78 (m, 1H), 3.25 (t, 2H), 2.90 (t, 2H), 2.82 (m, 2H), 2.25 (m, 2H), 1.90 (m, 2H), 1.84 (d, 3H), 1.60 (m, 2H).	584
II-142		ácido 2-dietilamino-etanosulfonico (4-{5-amino-6-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-pirazin-2-il}-fenil)-amida	0.22	3 como en el ejemplo I-243	(300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.70 (d, 2H), 7.28 (m, 2H), 7.21 (d, 2H), 7.01 (t, 1H), 6.82 (q, 1H), 5.05 (s, 2H), 3.20 (m, 2H), 2.85 (m, 2H), 2.28 (s, 3H), 1.83 (d, 3H).	528
II-143		ácido 2-((R)-3-hidroxi-pirrolidin-1-il)-etanosulfonico (4-{5-amino-6-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-pirazin-2-il}-fenil)-amida	0.19	3 como en el ejemplo I-243	(300 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.69 (d, 2H), 7.27 (m, 4H), 7.00 (t, 1H), 6.84 (q, 1H), 5.03 (s, 2H), 4.43 (m, 1H), 3.25 (m, 2H), 3.02 (m, 3H), 2.84 (m, 1H), 2.53 (m, 1H), 2.30 (m, 1H), 2.22 (m, 1H), 1.84 (d, 3H), 1.81 (m, 1H).	570
II-144		ácido 2-pirrolidin-1-il-etanosulfonico (4-{5-amino-6-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-pirazin-2-il}-fenil)-amida	0.36	3 como en el ejemplo I-243	(300 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.69 (d, 2H), 7.27 (m, 2H), 7.19 (d, 2H), 7.04 (t, 1H), 6.82 (q, 1H), 5.01 (s, 2H), 3.28 (m, 2H), 3.08 (m, 2H), 2.60 (m, 4H), 1.88 (m, 7H).	554
II-145		ácido 4-{5-amino-6-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-pirazin-2-il}-fenil)-benzoico	1.56	3 como en el ejemplo I-211		422

No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 146		4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- ((R)- 2- hidroxi- 3- pirrolidin- 1- il- propil)- benzamida	0.15	4 como en el ejemplo II- 146		548
II- 147		4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- ciclopropilamino- piperidin- 1- il)- metanona	0.13	4 como en el ejemplo II- 146		544
II- 148		4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- ((S)- 2- hidroxi- 3- pirrolidin- 1- il- propil)- benzamida	0.12	4 como en el ejemplo II- 146		548
II- 149		4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- ((R)- 2- hidroxi- 3- pirrolidin- 1- il- propil)- benzamida	0.13	4 como en el ejemplo II- 146		564
II- 150		4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4- il)- benzamida	0.068	4 como en el ejemplo II- 146	(300 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.78 (m, 4H), 7.28 (m, 1H), 6.95 (t, 1H), 6.80 (q, 1H), 5.95 (bd, 1H), 5.07 (s, 2H), 4.05 (m, 1H), 2.85 (m, 2H), 2.32 (s, 3H), 2.21 (m, 2H), 2.08 (m, 2H), 1.85 (d, 3H), 1.68 (m, 2H).	518
II- 151		4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.18	4 como en el ejemplo II- 146	(300 MHz, $CDCl_3$) δ 8.00 (d, 1H), 7.75 (d, 2H), 7.51 (d, 2R), 7.28 (m, 1H), 7.00 (t, 1H), 6.90 (q, 1H), 5.05 (s, 2H), 4.45 (m, 1H), 3.41 (m, 2H), 2.70 (m, 4H), 1.84 (d, 3H), 1.70- 2.0 (m, 10H)	558
II- 152		4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	0.11	4 como en el ejemplo II- 146	(300 MHz, $CDCl_3$) δ 7.00 (s, 1H), 7.75 (d, 2H), 7.40 (d, 2H), 7.28 (m, 1H), 6.99 (t, 1H), 5.76 (q, 1H) 5.04 (s, 2H), 4.64 (m, 1H), 3.64 (m, 1H), 3.02 (m, 2H), 2.60 (m, 4H), 2.30 (m, 1H), 1.92 (m, 1H), 1.81 (m, 6H), 1.69 (m, 2H), 1.62 (m, 2H).	558

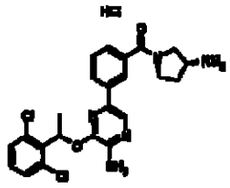
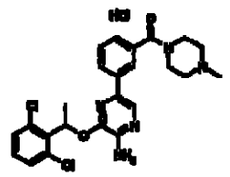
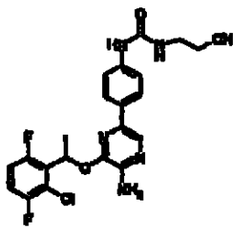
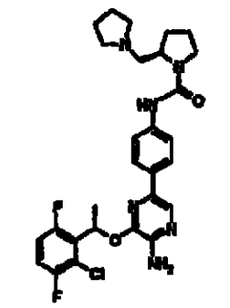
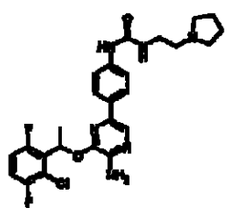
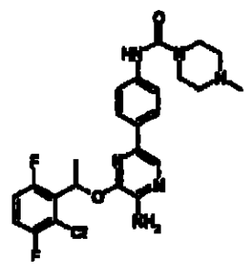
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H-NMR	MS m/z (M+1)
II-153		4-{5-amino-6-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-pirazin-2-il}-N-(2-morfolin-4-il-etil)-benzamida	0.102	4 como en el ejemplo II-146	(300 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.79 (m, 5H), 7.25 (m, 1H), 6.95 (t, 1H), 6.83 (q, 1H), 5.10 (s, 2H), 3.74 (m, 4H), 3.49 (m, 2H), 2.63 (m, 2H), 2.52 (m, 4H), 1.85 (d, 3H).	536
II-154		4-{5-amino-6-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-pirazin-2-il}-fenil)-(4-metil-piperazin-1-il)-metanona	0.16	4 como en el ejemplo II-146	(300 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.78 (d, 2H), 7.43 (d, 2H), 7.29 (m, 1H), 6.85 (t, 1H), 6.94 (q, 1H), 5.07 (s, 2H), 3.75 (m, 2H), 3.50 (m, 2H), 2.43 (m, 4H), 2.33 (s, 3H), 1.84 (d, 3H).	506
II-155		4-{5-amino-6-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-pirazin-2-il}-fenil)-((3R, 5S)-3,5-dimetil-piperazin-1-il)-metanona	0.095	4 como en el ejemplo II-146	(300 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.79 (d, 2H), 7.40 (d, 2H), 7.28 (m, 1H), 6.98 (t, 1H), 6.84 (q, 1H), 5.04 (s, 2H), 4.65 (m, 1H), 3.56 (m, 1H), 2.85 (m, 2H), 2.70 (m, 1H), 2.44 (m, 1H), 1.84 (d, 3H), 1.65 (m, 1H), 1.13 (m, 3H), 1.00 (m, 3H).	518
II-156		ácido 4-{5-amino-6-[1-(2,6-dicloro-3-fluoro-fenil)-etoxi]-pirazin-2-il}-benzoico		3 como en el ejemplo I-211		404
II-157		4-{5-amino-6-[1-(2,6-dicloro-fenil)-etoxi]-pirazin-2-il}-fenil)-(4-pirrolidin-1-il-piperidin-1-il)-metanona	0.16	4 como en el ejemplo II-157	(300 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.82 (d, 2H), 7.50 (d, 2H), 7.31 (d, 2H), 7.15 (t, 1H), 6.90 (q, 1H), 5.05 (s, 2H), 2.98 (br, 2H), 2.60 (s, 4H), 2.25 (br, 2H), 1.89 (d, 3H), 1.2-1.98 (br, 8H).	540
II-158		4-{5-amino-6-[1-(2,6-dicloro-fenil)-etoxi]-pirazin-2-il}-N-(2-morfolin-4-il-etil)-benzamida	0.32	4 como en el ejemplo II-157	(300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.89 (d, 2H), 7.75 (d, 2H), 7.32 (m, 2H), 7.15 (t, 1H), 6.91 (q, 1H), 6.78 (m, 1H), 5.10 (s, 2H), 3.74 (m, 4H), 3.63 (m, 2H), 2.65 (m, 2H), 2.54 (m, 4H), 1.85 (d, 3H).	516
II-159		4-{5-amino-6-[1-(2,6-dicloro-fenil)-etoxi]-pirazin-2-il}-fenil)-((3R, 5S)-3,5-dimetil-piperazin-1-il)-metanona	0.14	4 como en el ejemplo II-157	(300 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.82 (d, 2H), 7.50 (d, 2H), 7.31 (d, 2H), 7.15 (t, 1H), 6.90 (q, 1H), 5.05 (s, 2H), 4.60 (s, 1H), 4.30 (t, 1H), 3.60 (s, 1H), 2.70 (m, 4H), 1.89 (d, 3H), 0.8-1.2 (br, 6H).	500

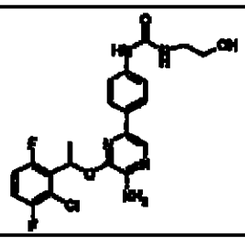
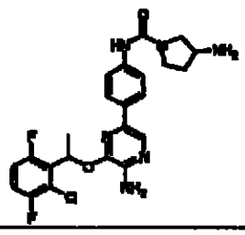
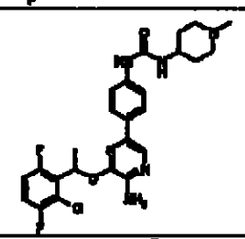
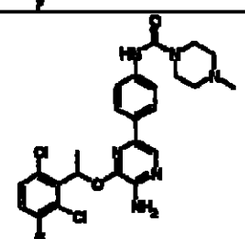
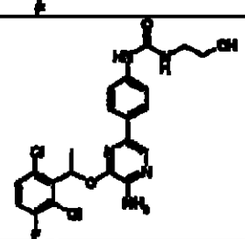
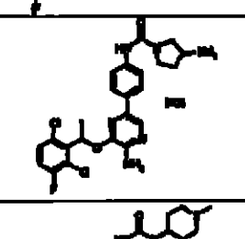
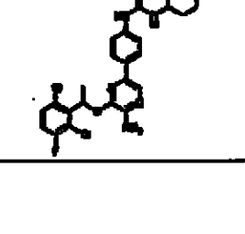
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 160		4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4- il)- benzamida	0.12	4 como en el ejemplo II- 157	(300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.90 (d, 2H), 7.83 (d, 2H), 7.32 (t, 2H), 7.16 (t, 1H), 6.84 (q, 1H), 6.00 (d, 1H), 5.08 (s, 2H), 4.05 (m, 1H), 2.81 (m, 2H), 2.35 (s, 3H), 2.21 (m, 2H), 2.08 (m, 2H), 1.84 (d, 3H), 1.60 (m, 2H).	500
II- 161		(4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.16	4 como en el ejemplo II- 157	(300 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.82 (d, 2H), 7.50 (d, 2H), 7.26 (d, 2H) 7.15 (t, 1H), 6.90 (q, 1H), 5.05 (s, 2H), 4.30 (t, 1H), 3.50 (m, 2H), 2.65 (m, 4H), 1.86 (d, 3H), 1.70- 2.0 (m, 10H)	542
II- 162		(4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.14	4 como en el ejemplo II- 157	(300 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.82 (d, 2H), 7.50 (d, 2H), 7.31 (d, 2H), 7.15 (t, 1H), 6.90 (q, 1H), 5.05 (s, 2H), 4.45 (m, 1H), 3.41 (m, 2H), 2.70 (m, 4H), 1.86 (d, 3H), 1.70- 2.0 (m, 10H)	542
II- 163		(4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- metil- piperazin- 1- il)- metanona	0.15	4 como en el ejemplo II- 157	(300 MHz, $CDCl_3$) δ 8.05 (s, 1 H), 7.82 (d, 2H), 7.50 (d, 2H), 7.31 (d, 2H), 7.15 (t, 1H), 6.90 (q, 1H), 5.05 (s, 2H), 3.60 (m, 4H), 2.45 (m, 4H), 2.31 (s, 3H), 1.89 (d, 3H)	486
II- 164		(4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((R)- 3- aminopirrolidin- 1- il)- metanona	0.15	4 como en el ejemplo II- 157	(300 MHz, CD_3OD) δ 7.89 (m, 3H), 7.60 (m, 2H), 7.40 (m, 2H), 7.25 (m, 1H), 6.74 (m, 1H), 4.90 (s, 2H), 4.05- 3.60 (m, 4H), 3.50 (m, 2H), 2.50 (m, 1H), 2.18 (m, 1H), 1.90 (d, 3H).	472
II- 165		Sal clorhídrica (4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((S)- 3- amino- pirrolidin- 1- il)- metanona	0.1	4 como en el ejemplo II- 157	(300MHZ, CD_3OD) δ 7.89 (m, 3h), 7.60 (m, 2H), 7.40 (m, 2H), 7.25 (m, 1H), 6.74 (m, 1H), 4.90 (s, 2H), 4.05- 3.60 (m, 4H), 3.50 (m, 2H), 2.50 (m, 1H), 2.18 (m, 1H), 1.90 (d, 3H).	472

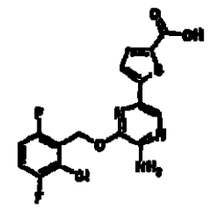
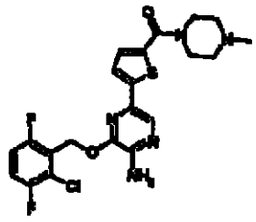
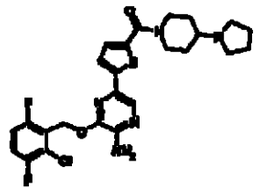
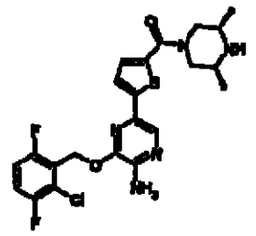
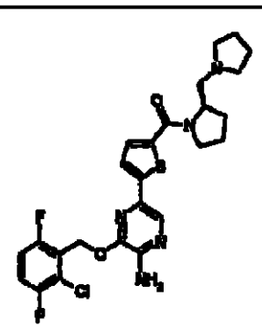
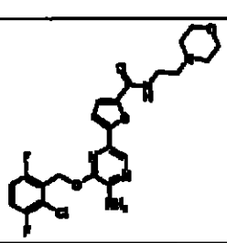
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 166		4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (2- pirrolidin- 1- il- etil)- benzamida	0.11	4 como en el ejemplo II- 157	(300 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.80 (m, 4H), 7.31 (dt, 2H), 7.16 (t, 1H), 6.84 (m, 2H), 5.04 (s, 2H), 3.55 (m, 2H), 2.71 (m, 2H), 2.57 (m, 4H), 1.84 (d, 3H), 1.83 (m, 4H).	502
II- 167		4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (3- pirrolidin- 1- il- propil)- benzamida	0.22	4 como en el ejemplo II- 157	(300 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.10 (s, 1H), 7.80 (m, 4H), 7.21 (d, 2H), 7.16 (t, 1H), 6.84 (q, 1H), 5.04 (s, 2H), 3.55 (m, 2H), 2.71 (m, 2H), 2.57 (m, 4H), 1.84 (m, 4H), 1.83 (d, 3H), 1.81 (m, 2H).	514
II- 168		ácido 3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- benzoico		3 como en el ejemplo I- 211		404
II- 169		3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4- il)- benzamida	0.18	4 como en el ejemplo II- 169	(300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 8.03 (s, 1H), 7.88 (d, 1H), 7.70 (d, 1H), 7.42 (t, 1H), 7.28 (d, 2H), 7.10 (t, 1H), 6.94 (q, 1H), 6.15 (bd, 1H), 5.08 (s, 2H), 4.05 (m, 1H), 2.91 (m, 2H), 2.35 (s, 3H), 2.21 (m, 2H), 2.08 (m, 2H), 1.84 (d, 3H), 1.68 (m, 2H).	502
II- 170		3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (2- pirrolidin- 1- il- etil)- benzamida	0.33	4 como en el ejemplo II- 169	(300 MHz, $CDCl_3$) δ 8.15 (s, 1 H), 8.02 (s, 1H), 7.85 (d, 1H), 7.71 (d, 1H) 7.40 (t, 1H) 7.28 (d, 2H), 7.10 (m, 2H), 6.90 (q, 1H), 5.10 (s, 2H), 3.64 (m, 2H), 2.80 (m, 2H), 2.64 (m, 4H), 1.85 (m, 7H).	500
II- 171		(3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((3R, 5R)- 3,5- dimetil- piperazin- 1- il)- metanona	0.36	4 como en el ejemplo II- 169	(300 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.79 (m, 2H), 7.40 (t, 1H), 7.28 (m, 3H), 7.11 (t, 1H), 6.86 (q, 1H), 5.05 (s, 2H), 4.69 (m, 1H), 3.56 (m, 1H), 2.95 (m, 1H), 2.79 (m, 1H), 2.71 (m, 1H), 2.44 (m, 1H), 1.84 (d, 3H), 1.25 (d, 3H), 1.17 (d, 3H).	500
II- 172		3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- benzamida	0.48	4 como en el ejemplo II- 169	(300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 8.03 (s, 1H), 7.89 (d, 1H), 7.69 (d, 1H), 7.43 (t, 1H), 7.28 (d, 2H), 7.10 (t, 1H), 6.91 (q, 1H), 6.88 (m, 1H), 5.10 (s, 2H), 3.74 (m, 4H), 3.63 (m, 2H), 2.65 (m, 2H), 2.54 (m, 4H), 1.85 (d, 3H).	516

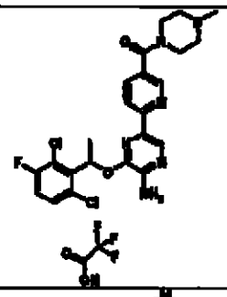
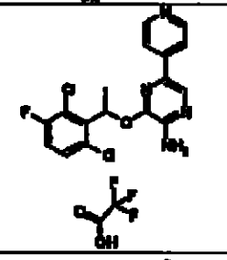
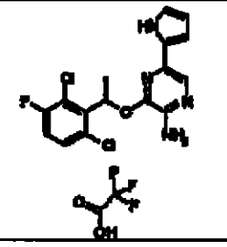
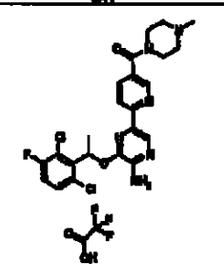
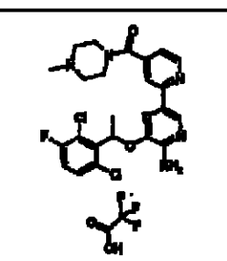
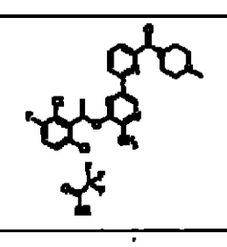
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 173		(3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.18	4 como en el ejemplo II- 169	(300 MHz, $CDCl_3$) δ 8.01 (d, 1H), 7.87 (m, 2H), 7.37 (m, 2H), 7.28 (m, 2H), 7.11 (t, 1H), 6.90 (m, 1H), 5.05 (s, 2H), 4.45 (m, 1H), 3.41 (m, 2H), 2.70 (m, 4H), 1.84 (d, 3H), 1.70- 2.0 (m, 10H)	540
II- 174		(3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	0.17	4 como en el ejemplo II- 169	(300 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.78 (m, 2H), 7.39 (t, 1H), 7.28 (m, 3H), 7.08 (t, 1H), 6.87 (q, 1H), 5.04 (s, 2H), 4.64 (m, 1H), 3.84 (m, 1H), 3.02 (m, 2H), 2.60 (m, 4H), 2.30 (m, 1H), 1.92 (m, 1H), 1.81 (m, 6H), 1.69 (m, 2H), 1.62 (m, 2H).	540
II- 175		N- [2- (4- acetil- piperazin- 1- il)- etil]- 4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- benzamida	0.28	4 como en el ejemplo II- 169	(300 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.89 (d, 2H), 7.75 (d, 2H), 7.31 (dt, 2H), 7.11(t, 1H), 6.91 (q, 1H), 6.78 (m, 1H), 5.12 (s, 2H), 4.25 (t, 1H), 3.60 (m, 3H), 3.45 (m, 1H), 2.65 (t, 2H), 2.50 (m, 3H), 2.05 (s, 2H), 1.85 (d, 3H).	559
II- 176		N- [2- (4- acetil- piperazin- 1- il)- etil]- 3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- benzamida	0.35	4 como en el ejemplo II- 169	(300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 8.03 (s, 1H), 7.99 (d, 1H), 7.69 (d, 1H), 7.43 (t, 1H), 7.28 (d, 2H), 7.11 (t, 1H), 6.91 (q, 1H), 6.78 (m, 1H), 5.12 (s, 2H), 3.65 (m, 4H), 3.49 (m, 2H), 2.68 (m, 2H), 2.54 (m, 4H), 2.09 (s, 3H), 1.85 (d, 3H).	559
II- 177		(3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.33	4 como en el ejemplo II- 169	(300 MHz, $CDCl_3$) δ 8.01 (d, 1H), 7.87 (m, 2H), 7.37 (m, 2H), 7.28 (m, 2H), 7.11 (t, 1H), 6.90 (m, 1H), 5.05 (s, 2H), 4.45 (m, 1H), 3.41 (m, 2H), 2.70 (m, 4H), 1.84 (d, 3H), 1.70- 2.0 (m, 10H)	540
II- 178		3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (3- pirrolidin- 1- il- propil)- benzamida	0.34	4 como en el ejemplo II- 169	(300 MHz, $CDCl_3$) δ 8.48 (m, 1H), 8.22 (t, 1H), 8.05 (s, 1H), 7.91 (dt, 1H), 7.66 (d, 1H), 7.40 (t, 1H), 7.28 (d, 2H), 7.10 (t, 1H), 6.94 (q, 1H), 5.04 (s, 2H), 3.62 (m, 2H), 2.71 (m, 2H), 2.57 (m, 4H), 1.84 (d, 3H), 1.83 (m, 2H), 1.81 (m, 4H).	514
II- 179		(3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((S)- 3- amino- pirrolidin- 1- il)- metanona	0.11	4 como en el ejemplo II- 169	(300 MHz, CD_3OD) δ 7.83 (m, 3H), 7.48 (m, 2H), 7.37 (m, 2H), 7.23 (m, 1H), 6.74 (m, 1H), 4.05- 3.60 (m, 4H), 3.50 (m, 1H), 2.50 (m, 1H), 2.18 (m, 1H), 1.90 (d, 3H).	472

1182

No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 180		Sal clorhídrica (3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona	0.18	4 como en el ejemplo II- 169	(300 MHz, CD_3OD) δ 7.83 (m, 3H), 7.48 (m, 2H), 7.37 (m, 2H), 7.23 (m, 1H), 6.74 (m, 1H), 4.05- 3.60 (m, 4H), 3.50 (m, 1H), 2.50 (m, 1H), 2.18 (m, 1H), 1.90 (d, 3H).	472
II- 181		(3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- metil- piperazin- 1- il)- metanona	0.25	4 como en el ejemplo II- 169	(300 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.80 (m, 2H), 7.40 (t, 1H), 7.28 (m, 3H), 7.11 (t, 1H), 6.87 (q, 1H), 5.05 (a, 2H), 4.64 (m, 1H), 3.87 (m, 2H), 3.45 (m, 2H), 2.53 (m, 2H), 2.36 (m, 1H), 2.34 (s, 3H), 1.84 (d, 3H).	486
II- 182		1- (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- 3- (2- morfolin- - 4- il- etil)- urea	0.18	10 como en el ejemplo I- 371	(300 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.68 (d, 2H), 7.38 (s, 2H), 6.95 (m, 4H), 6.70 (q, 1H), 4.94 (S, 2H), 3.75 (m, 4H), 3.46 (m, 2H), 2.69 (m, 4H), 2.26 (m, 2H), 1.85 (d, 3H).	534
II- 183		ácido (R)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxílico (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida	0.21	10 como en el ejemplo I- 371	(300 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.40 (d, 2H), 7.27 (d, 2H), 6.95 (m, 3H), 5.95 (q, 1H), 4.85 (s, 2H), 3.85 (m, 1H), 3.75 (m, 1H), 3.40 (m, 1H), 2.90 (m, 4H), 2.65 (m, 4H), 2.10 (m, 3H), 1.85 (d, 3H), 1.9- 1.7 (m, 3H).	557
II- 184		1- (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- 3- (2- pirrolidin- 1- il- etil)- urea	0.18	10 como en el ejemplo I- 371	(300 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.80 (bs, 1H), 7.69 (d, 2H), 7.46 (d, 2H), 7.35 (bm, 1H), 7.05 (m, 2H), 6.72 (q, 1H), 4.86 (s, 2H), 3.58 (m, 2H), 3.19 (m, 4H), 3.12 (m, 2H), 2.16 (m, 4H), 2.51 (s, 3H), 1.81 (d, 3H).	517
II- 185		ácido 4- metil- piperazina- 1- carboxílico (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida	0.1	10 como en el ejemplo I- 371	(300 MHz, $CDCl_3$) δ 7.95 (s, 1 H), 7.69 (d, 2H), 7.39 (d, 2H), 7.01- 6.91 (m, 2H), 6.70 (m, 2H), 4.90 (s, 2H), 3.61 (m, 4H), 2.58 (m, 4H), 2.41 (s, 3H), 1.81 (d, 3H).	503

No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 186		1- (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- 3- (2- hidroxi- etil)- urea	0.21	10 como en el ejemplo I- 371	(300 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.60 (d, 2H), 7.35 (d, 2H), 7.15 (m, 4H), 6.55 (q, 1H), 4.86 (s, 2H), 3.64 (t, 2H), 3.31 (t, 3H), 1.82 (d, 3H).	564
II- 187		ácido (S)- 3- amino- pirrolidina- 1- carboxílico (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida	0.082	10 como en el ejemplo I- 371	(300 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.65 (d, 2H), 7.53 (d, 2H), 7.15 (m, 3H), 6.77 (m, 1H), 4.87 (s, 2H), 3.95 (m, 1H), 3.80 (m, 1H), 3.65 (m, 2H), 3.31 (m, 2H), 2.57 (m, 1H), 2.20 (m, 1H), 1.95 (d, 3H).	489
II- 188		1- (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- 3- (1- metil- piperidin- 4- il)- urea	0.054	10 como en el ejemplo I- 371		517
II- 189		ácido 4- metil- piperazina- 1- carboxílico (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida	0.074	10 como en el ejemplo I- 371	(300 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.66 (d, 2H), 7.37 (d, 2H), 7.24 (m, 1H), 6.95 (t, 1H), 6.81 (m, 2H), 4.95 (s, 2H), 3.68 (m, 4H), 2.73 (m, 4H), 2.51 (s, 3H), 1.83 (d, 3H).	519
II- 190		1- (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- 3- (2- hidroxi- etil)- urea	0.28	10 como en el ejemplo I- 371	(300 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.60 (m, 4H), 7.33 (m, 3H), 7.15 (m, 1H), 6.70 (q, 1H), 4.86 (s, 2H), 3.64 (t, 2H), 3.31 (m, 3H), 1.82 (d, 3H).	480
II- 191		ácido (S)- 3- amino- pirrolidina- 1- carboxílico (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida	3	10 como en el ejemplo I- 371		502
II- 192		1- (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- 3- (1- metil- piperidin- 4- il)- urea	0.052	10 como en el ejemplo I- 371		535

No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 193		ácido 5- [5- amino- 6- [2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofeno- 2- carboxílico		3 como en el ejemplo I- 270		398
II- 194		{5- [5- amino- 6- [2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofeno- 2- il}- (4- metil- piperazin- 1- il)- metanona	0.62	4 como en el ejemplo II- 194	(300 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.35 (s, 1H), 7.27 (s, 1H), 7.15 (m, 1H), 6.98 (m, 1H), 5.63 (s, 1H), 4.87 (m, 1H), 3.80 (m, 4H), 2.48 (m, 4H), 2.34 (s, 3H).	480
II- 195		{5- [5- amino- 6- [2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofeno- 2- il}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona	0.51	4 como en el ejemplo II- 194	(300 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.35 (d, 1H), 7.24 (d, 1H), 7.15 (m, 1H), 6.98 (m, 1H), 5.63 (s, 2H), 4.88 (m, 2H), 4.42 (m, 4H), 3.05 (t, 4H), 2.63 (m, 2H), 2.35 (m, 1H), 2.00 (m, 2H), 1.82 (m, 2H), 1.60 (m, 2H).	534
II- 196		{5- [5- amino- 6- [2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofeno- 2- il}- ((3R- 5S)- 3,5- dimetil- piperazin- 1- il)- metanona	0.55	4 como en el ejemplo II- 194	(300 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.35 (d, 1H), 7.24 (d, 1H), 7.07 (m, 1H), 7.01 (m, 1H), 5.63 (s, 2H), 4.88 (m, 2H), 4.35 (m, 2H), 2.93 (m, 2H), 2.60 (m, 2H) 1.10 (d, 6H).	494
II- 197		{5- [5- amino- 6- [2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofeno- 2- il}- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona	0.8	4 como en el ejemplo II- 194	(300 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.52 (d, 1H), 7.38 (d, 1H), 7.07 (m, 1H), 7.01 (m, 1H), 5.63 (s, 2H), 4.88 (m, 2H), 4.5- 0.80 (m, 17H)	534
II- 198		ácido {5- [5- amino- 6- [2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofeno- 2- carboxílico (4- morfolin- 4- il- etil)- amida	0.7	4 como en el ejemplo II- 194	(300 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.45 (d, 1H), 7.38 (d, 1H), 7.20 (m, 1H), 7.05 (m, 1H), 6.58 (m, 1H), 5.65 (s, 2H), 4.89 (m, 2H), 3.75 (m, 4H), 3.55 (m, 2H), 2.61 (m, 2H), 2.50 (m, 4H)	510

No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 199		trifluoroacetato de 3- [1- (2,6- dicloro- 3- fluoro- fenil)etoxi]- 5- {5- [(4- metilpiperazin- 1- il)carbonil]piridin- 2- il}- pirazin- 2- amina	0.15	4 como en el ejemplo II- 194	(DMSO- d6+TFA/300 MHz) δ 8.64 (s, 1H), 8.29 (s, 1H), 7.96 (d, 1H), 7.81 (d, 1H), 7.51 (m, 1H), 7.35 (m, 1H), 6.63 (q, 1H), 4.69- 4.25 (m, 1H), 4.08- 3.69 (m, 1H), 3.58- 3.01 (m, 6H), 2.82 (s, 3H), 1.84 (d, 3H).	505
II- 200		3- [1- (2,6- dicloro- 3- fluoro- fenil)-.etoxi]- 5- piridin- 4- il- pirazin- 2- ilamina	0.045	3		379
II- 201		3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (1H- pirrol- 2- il)- pirazin- 2- ilamina	0.22	3		367
II- 202		(6- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- piridin- 3- il)- (4- metil- piperazin- 1- il)- metanona	0.15	16 como en el ejemplo I- 488		505
II- 203		(2- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- piridin- 4- il)- (4- metil- piperazin- 1- il)- metanona	0.18	16 como en el ejemplo I- 488	(DMSO- d6+TFA/300 MHz) δ 8.68 (d, 1H), 8.34 (s, 1H), 7.62 (s, 1H), 7.52- 7.27 (m, 3H), 6.57 (q, 1H), 4.66 (m, 1H), 3.70- 2.91 (m, 7H), 2.86 (s, 3H), 1.82 (d, 3H).	505
II- 204		(6- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- piridin- 2- il)- (4- metil- piperazin- 1- il)- metanona	0.22	16 como en el ejemplo I- 488	(DMSO- d6+TFA/300 MHz) δ 8.24 (s, 1H), 7.96 (dd, 1H), 7.79 (d, 1H), 7.53 (m, 2H), 7.35 (dd, 1H), 6.61 (q, 1H), 4.60 (br, 1H), 4.12 (br, 1H), 3.61- 3.30 (m, 3H), 3.24- 3.04 (m, 3H), 2.83 (s, 3H), 1.84 (d, 3H).	505

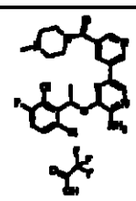
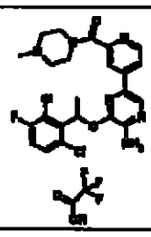
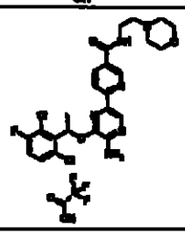
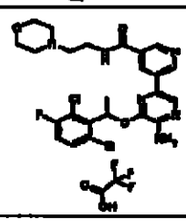
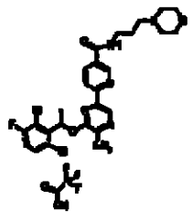
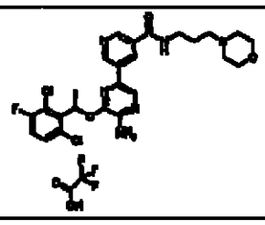
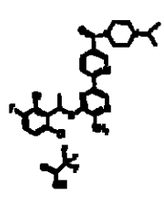
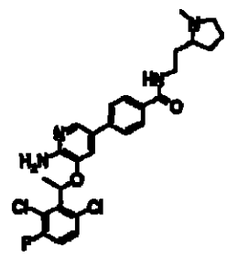
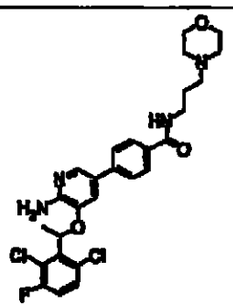
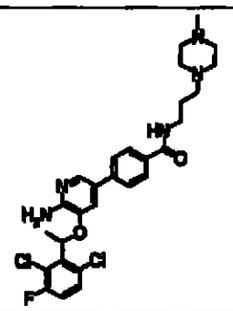
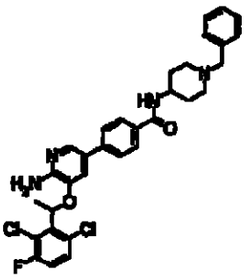
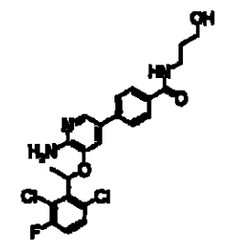
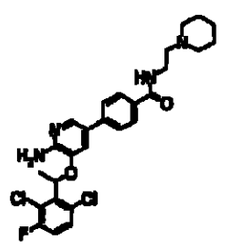
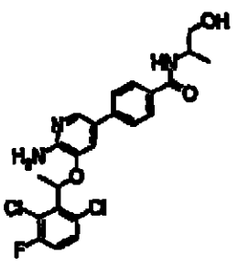
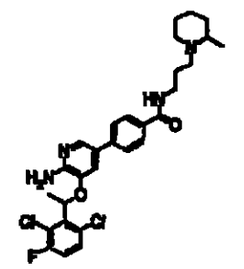
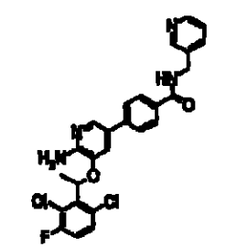
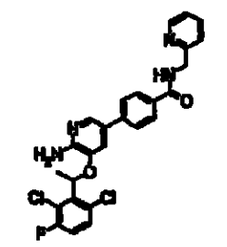
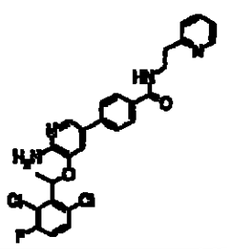
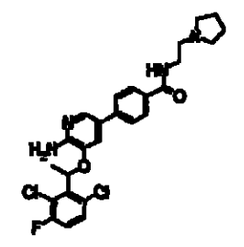
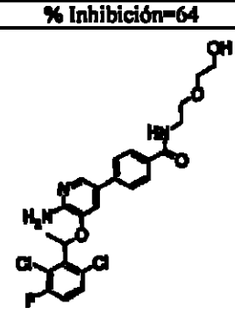
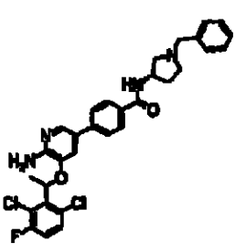
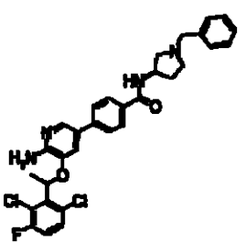
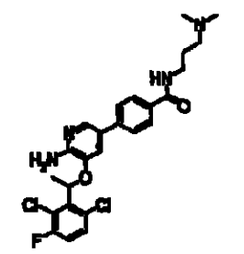
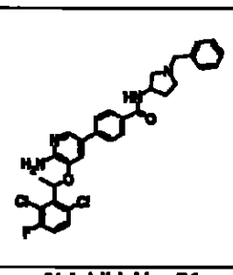
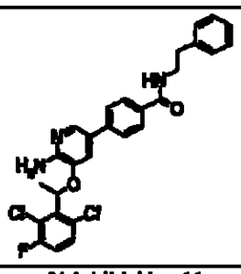
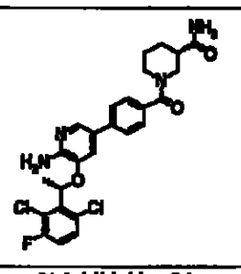
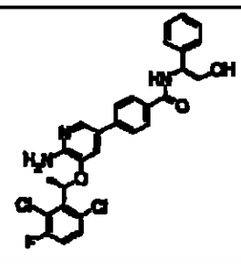
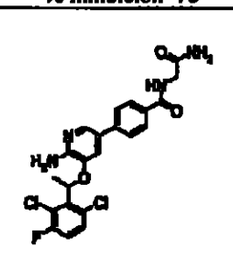
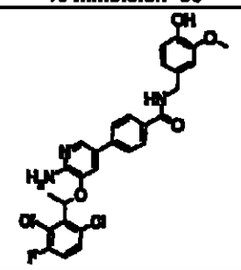
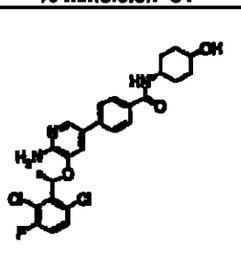
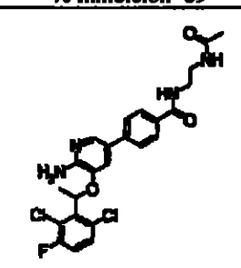
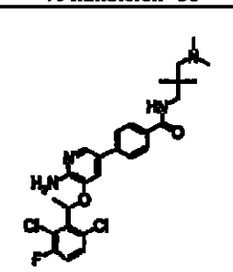
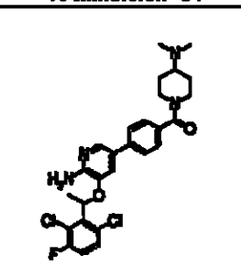
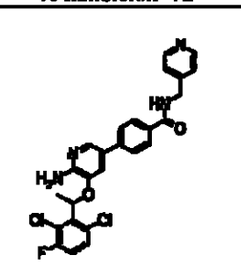
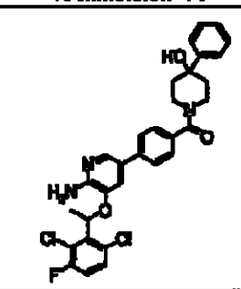
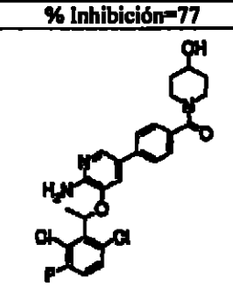
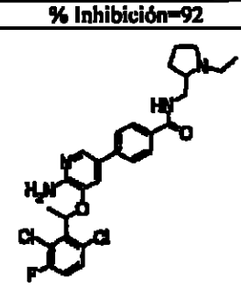
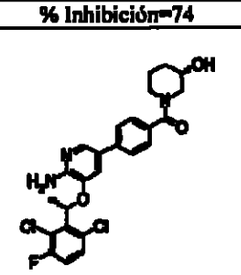
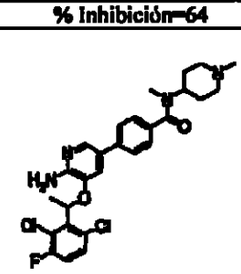
No.	Estructura	Nombre	Met IC_{50} (μM)	Procedimiento	^{1}H- NMR	MS m/z (M+1)
II- 205		(5- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- piridin- 3- il)- (4- metil- piperazin- 1- il)- metanona	0.1	16 como en el ejemplo I- 488	(DMSO- d6+TFA/300 MHz) δ 9.07 (s, 1H), 8.77 (s, 1H), 8.44 (s, 1H), 8.31 (s, 1H), 7.53 (br, 1H), 7.44 (m, 1H), 7.32 (m, 1H), 6.58 (q, 1H), 4.63 (br, 1H), 3.74 (br, 1H), 3.61- 3.15 (m, 4H), 3.06 (m, 2H), 2.83 (s, 3H), 1.81 (d, 3H).	505
II- 206		(4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- piridin- 2- il)- (4- metil- piperazin- 1- il)- metanona	0.1	16 como en el ejemplo I- 488	(DMSO- d6+TFA/300 MHz) δ 8.63 (d, 1H), 8.39 (s, 1H), 8.01 (s, 1H), 7.93 (d, 1H), 7.43 (m, 1H), 7.28 (dd, 1H), 6.58 (q, 1H), 4.63 (m, 1H), 3.92 (m, 1H), 3.64- 3.13 (m, 4H), 3.11- 2.96 (m, 2H), 2.84 (s, 3H), 1.81 (d, 3H).	505
II- 207		6- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- nicotinamida		16 como en el ejemplo I- 488	(DMSO- d6+TFA/300 MHz) δ 9.76 (br, 1H), 8.96 (m, 2H), 8.37 (s, 1H), 8.26 (d, 1H), 7.80 (d, 1H), 7.51 (m, 1H), 7.37 (dd, 1H), 6.61 (q, 1H), 4.00 (d, 2H), 3.74- 3.50 (m, 6H), 3.34 (m, 2H), 3.16 (m, 2H), 1.83 (d, 3H).	535
II- 208		5- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- nicotinamida	0.038	16 como en el ejemplo I- 488	(DMSO- d6+TFA/300 MHz) δ 9.16 (m, 1H), 9.09 (s, 1H), 9.03 (s, 1H), 8.83 (s, 1H), 8.28 (s, 1H), 7.47 (m, 1H), 7.32 (dd, 1H), 6.66 (q, 1H), 4.00 (d, 2H), 3.77- 3.50 (m, 6H), 3.35 (m, 2H), 3.16 (m, 2H), 1.83 (d, 3H).	535
II- 209		6- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- morfolin- 4- il- propil)- nicotinamida		16 como en el ejemplo I- 488	(DMSO- d6+TFA/300 MHz) δ 9.74 (br, 1H), 8.97 (s, 1H), 8.84 (m, 1H), 8.36 (s, 1H), 8.26 (d, 1H), 7.79 (d, 1H), 7.50 (m, 1H), 7.37 (dd, 1H), 6.61 (q, 1H), 3.97 (d, 2H), 3.64 (t, 2H), 3.50- 3.30 (m, 4H), 3.23- 2.98 (m, 4H), 1.92 (m, 2H), 1.83 (d, 3H).	549
II- 210		5- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- morfolin- 4- il- propil)- nicotinamida	0.022	16 como en el ejemplo I- 488	(DMSO- d6+TFA/300 MHz) δ 9.88 (br, 1H), 8.86 (s, 1H), 8.30 (s, 1H), 7.68- 7.40 (m, 2H), 7.32 (m, 1H), 6.67 (q, 1H), 3.97 (d, 2H), 3.66 (t, 2H), 3.43 (m, 4H), 3.25- 2.97 (m, 4H), 1.96 (br, 2H), 1.83 (d, 3H).	549
II- 211		(6- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- piridin- 3- il)- (4- isopropil- piperazin- 1- il)- metanona		16 como en el ejemplo I- 488	(DMSO- d6+TFA/300 MHz) δ 9.70 (br, 1H), 8.65 (s, 1H), 8.38 (s, 1H), 7.95 (d, 1H), 7.80 (d, 1H), 7.53 (m, 1H) 7.39 (dd, 1H), 6.62 (q, 1H), 4.57 (br, 1H), 3.85 (br, 1H), 3.60- 3.05 (m, 7H), 1.83 (d, 3H), 1.26 (d, 6H).	533

Tabla 5

Sección A: Ejemplos L- 1 a L- 16

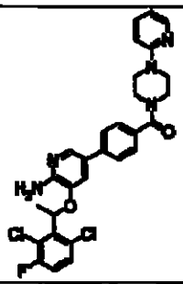
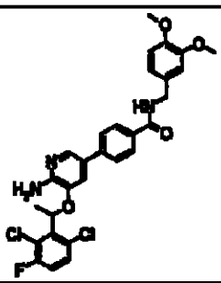
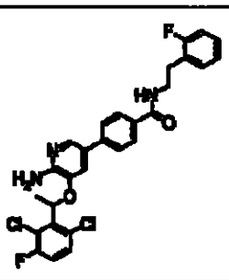
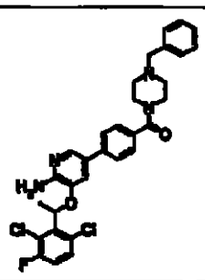
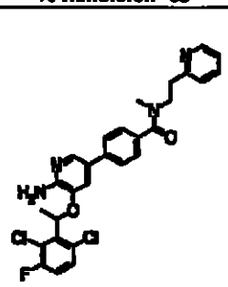
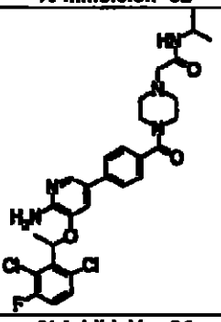
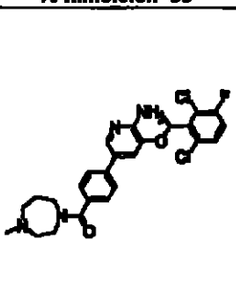
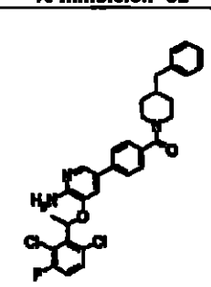
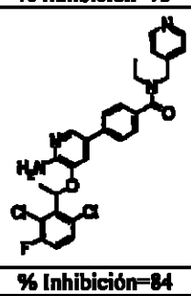
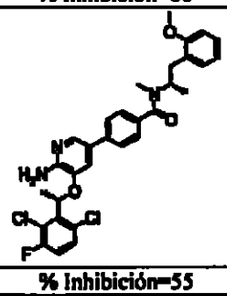
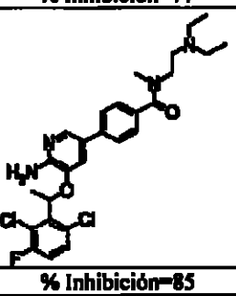
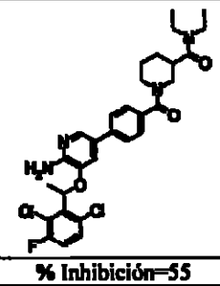
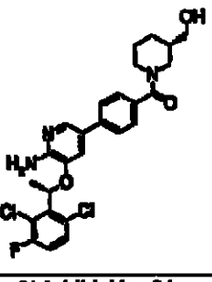
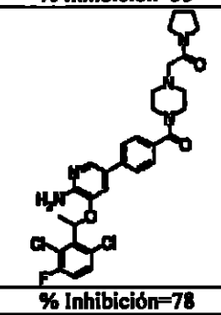
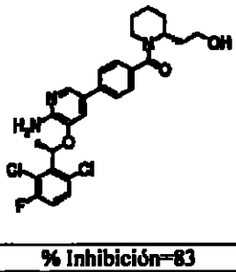
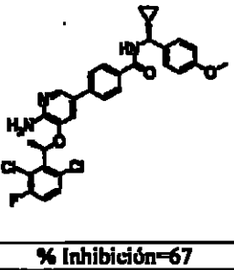
			
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% Inhibición=68	% Inhibición=69	% Inhibición=66	% Inhibición=72
			
% Inhibición=64	% Inhibición=67	% Inhibición=67	% Inhibición=82
			
% Inhibición=76	% Inhibición=72	% Inhibición=67	% Inhibición=83

Sección B: Ejemplos L- 17 a L- 32

			
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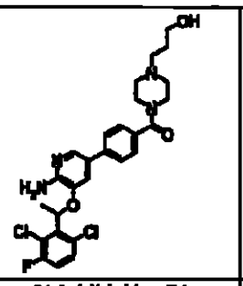
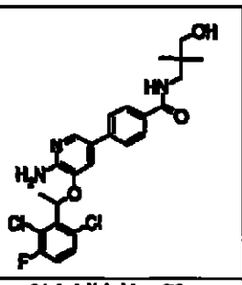
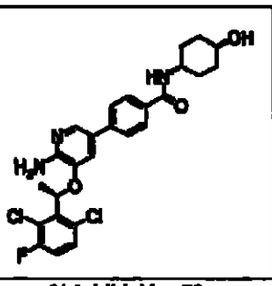
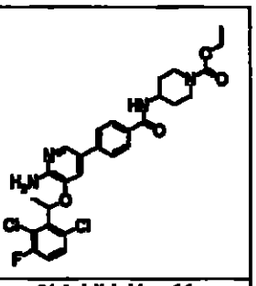
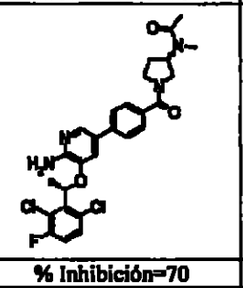
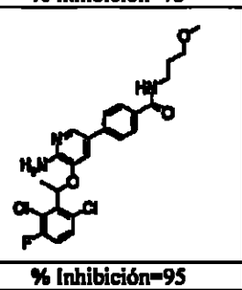
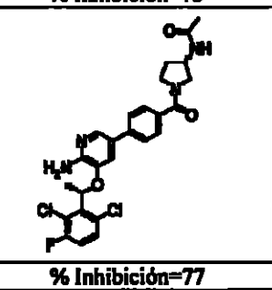
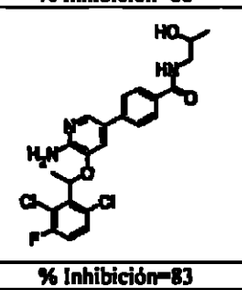
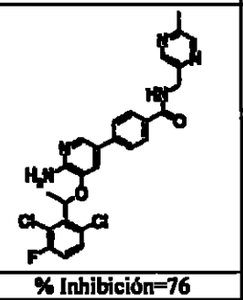
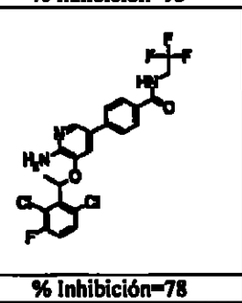
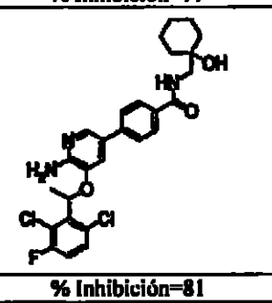
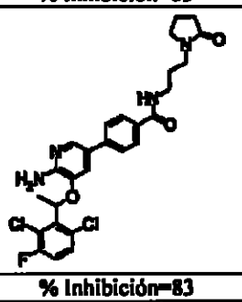
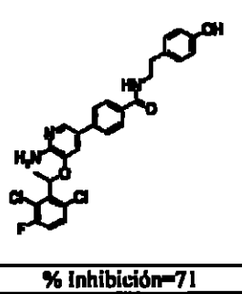
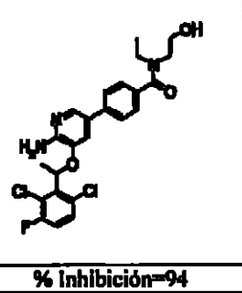
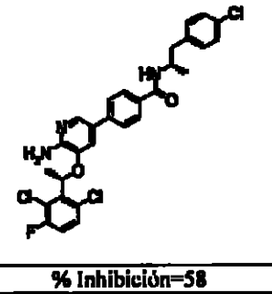
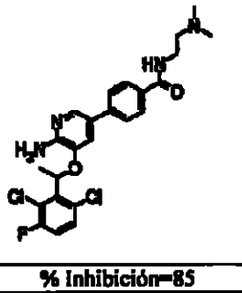
5

Sección C: Ejemplos L- 33 a L- 48

			
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% Inhibición=75	% Inhibición=86	% Inhibición=77	% Inhibición=55
			
% Inhibición=84	% Inhibición=55	% Inhibición=85	% Inhibición=55
			
% Inhibición=84	% Inhibición=78	% Inhibición=83	% Inhibición=67

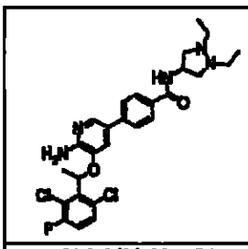
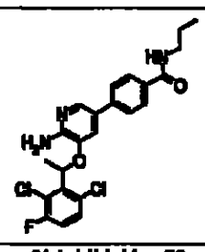
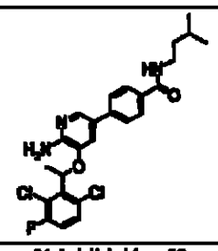
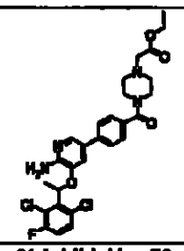
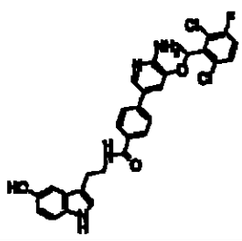
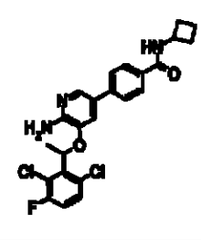
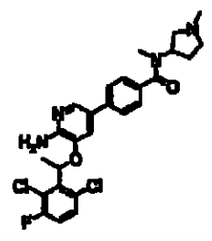
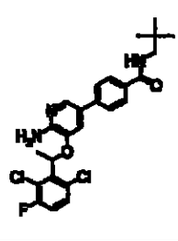
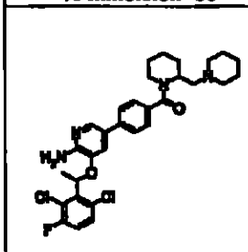
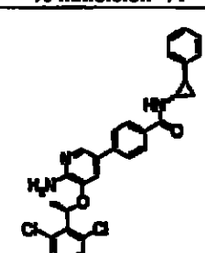
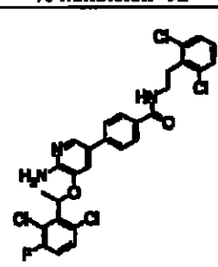
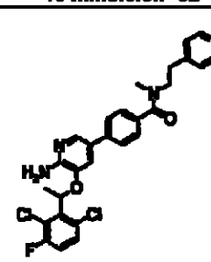
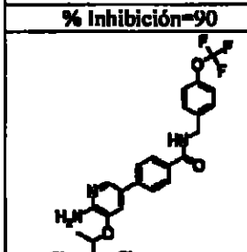
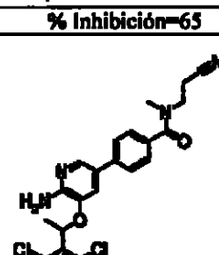
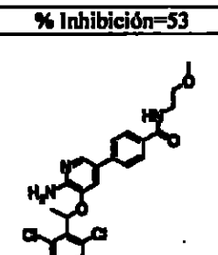
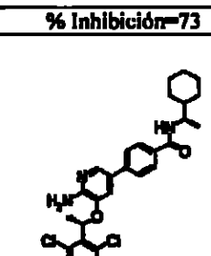
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Sección D: Ejemplos L- 49 a L- 64

			
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% Inhibición=70	% Inhibición=95	% Inhibición=77	% Inhibición=83
			
% Inhibición=76	% Inhibición=78	% Inhibición=81	% Inhibición=83
			
% Inhibición=71	% Inhibición=94	% Inhibición=58	% Inhibición=85

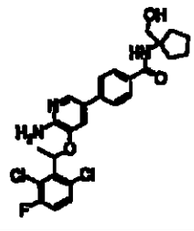
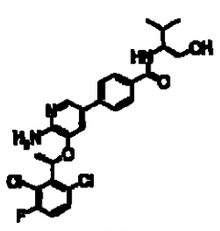
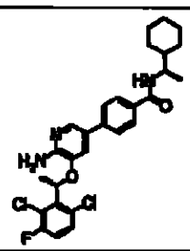
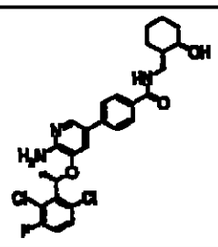
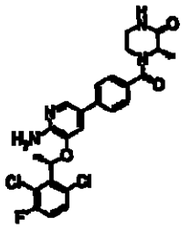
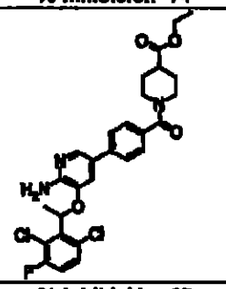
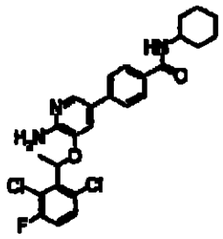
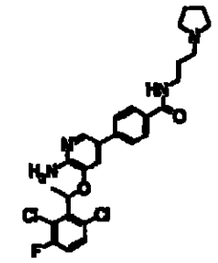
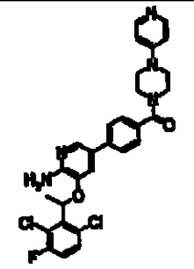
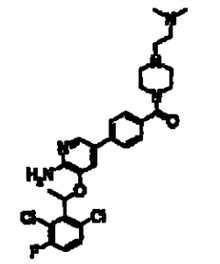
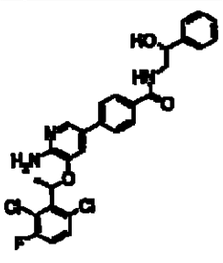
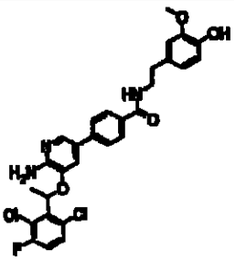
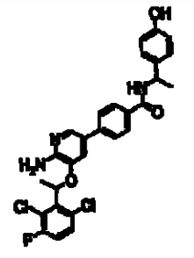
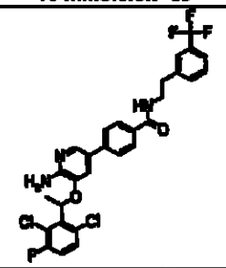
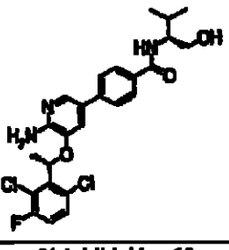
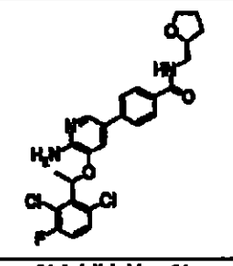
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Sección E: Ejemplos L- 65 a L- 80

			
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% Inhibición=66	% Inhibición=71	% Inhibición=92	% Inhibición=62
			
% Inhibición=90	% Inhibición=65	% Inhibición=53	% Inhibición=73
			
% Inhibición=54	% Inhibición=68	% Inhibición=73	% Inhibición=60

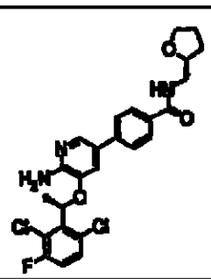
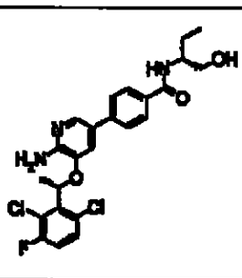
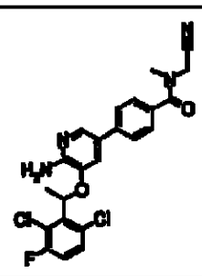
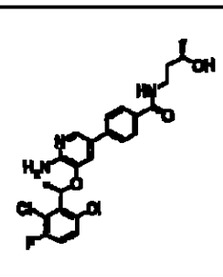
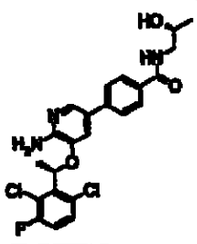
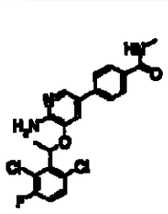
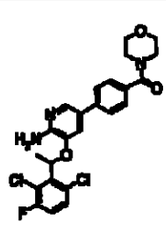
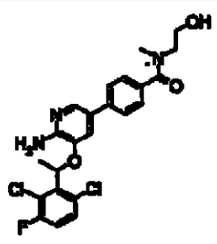
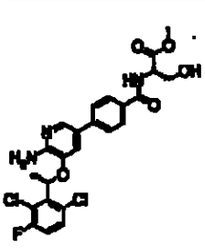
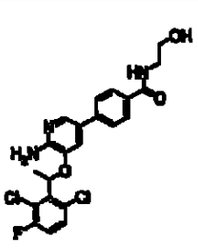
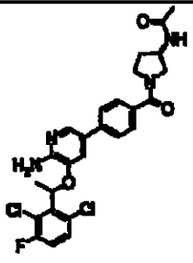
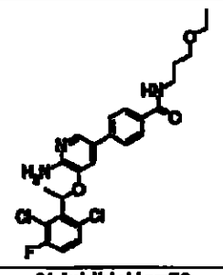
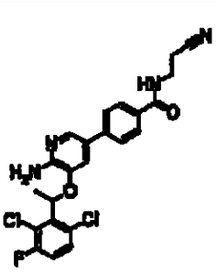
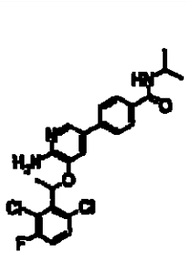
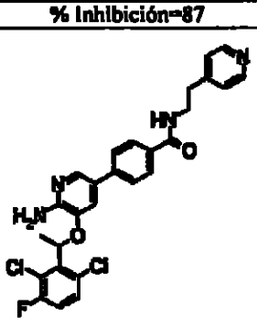
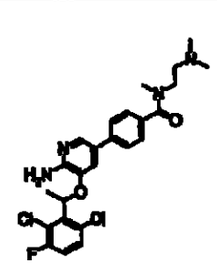
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Sección F: Ejemplos L- 81 a L- 96

			
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% Inhibición=86	% Inhibición=57	% Inhibición=56	% Inhibición=90
			
% Inhibición=96	% Inhibición=85	% Inhibición=69	% Inhibición=64
			
% Inhibición=62	% Inhibición=51	% Inhibición=65	% Inhibición=61

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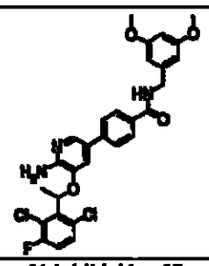
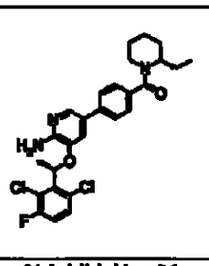
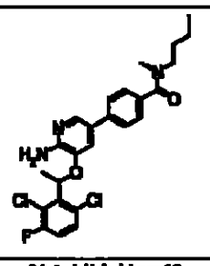
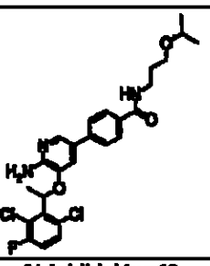
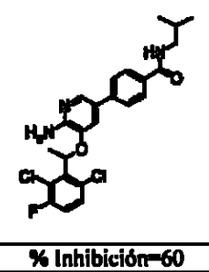
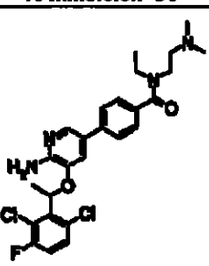
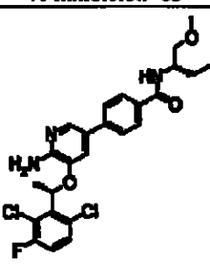
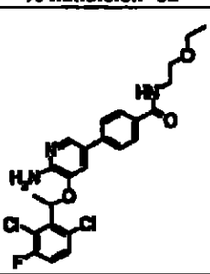
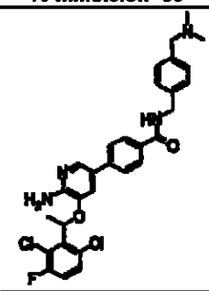
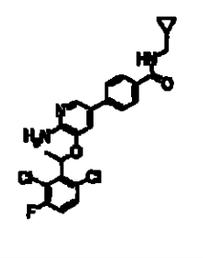
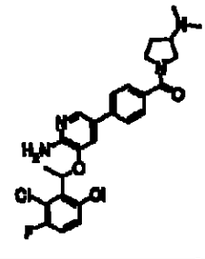
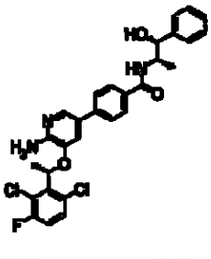
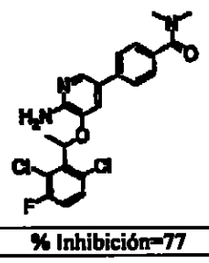
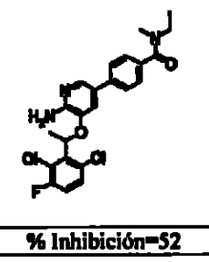
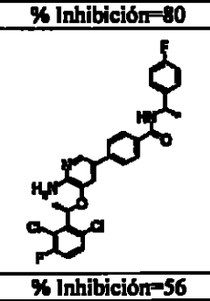
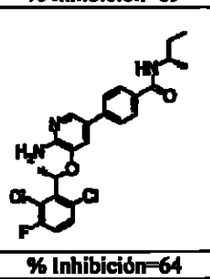
Sección G: Ejemplos L- 97 a L- 112

			
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% Inhibición=79	% Inhibición=82	% Inhibición=91	% Inhibición=89
			
% Inhibición=81	% Inhibición=89	% Inhibición=87	% Inhibición=70
			
% Inhibición=76	% Inhibición=71	% Inhibición=71	% Inhibición=85

5

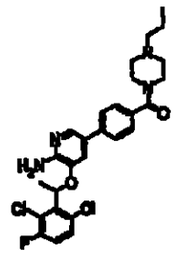
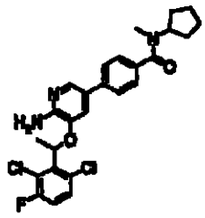
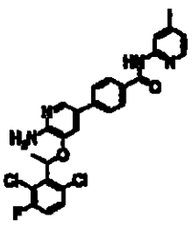
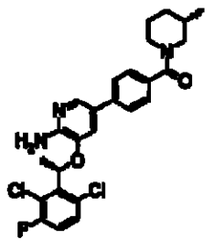
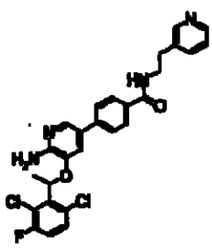
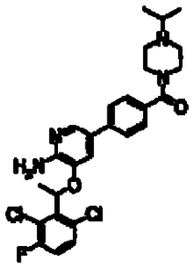
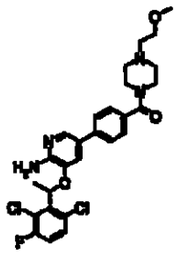
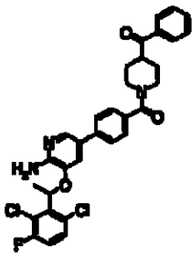
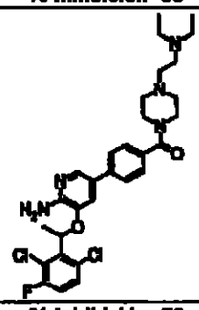
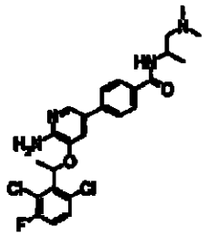
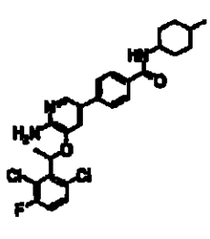
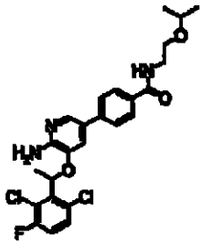
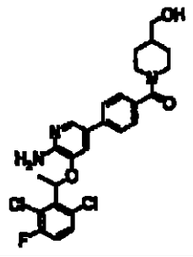
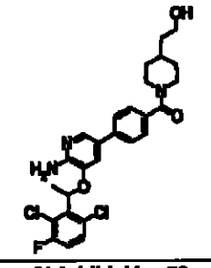
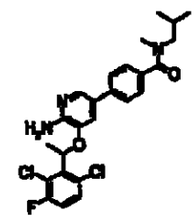
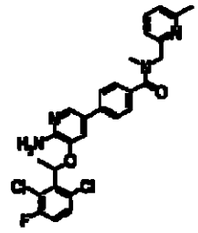
10

Sección H: Ejemplos L- 113 a L- 128

			
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% Inhibición=60	% Inhibición=86	% Inhibición=59	% Inhibición=63
			
% Inhibición=75	% Inhibición=61	% Inhibición=80	% Inhibición=69
			
% Inhibición=77	% Inhibición=52	% Inhibición=56	% Inhibición=64

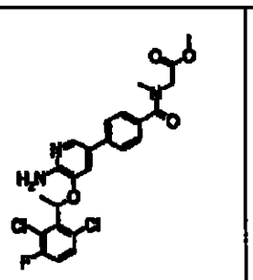
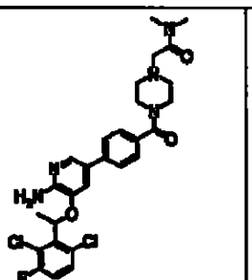
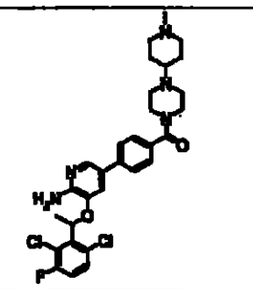
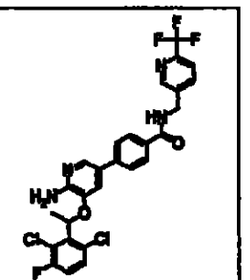
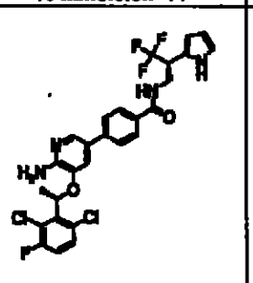
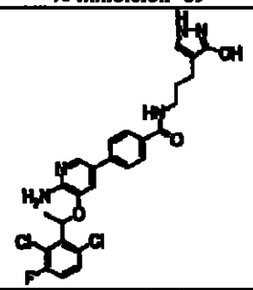
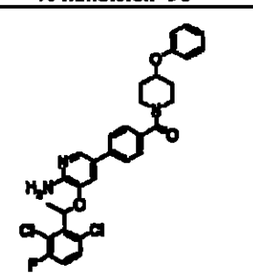
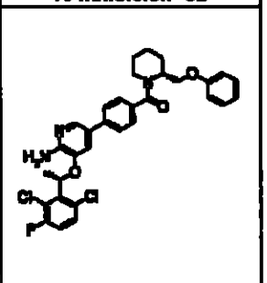
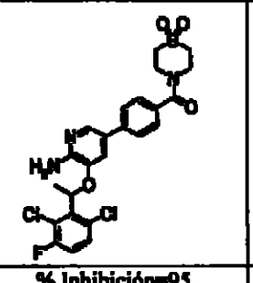
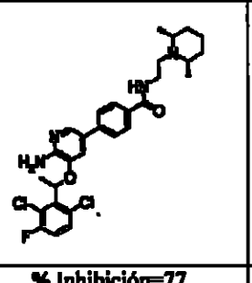
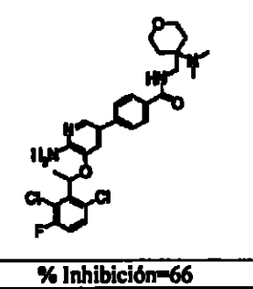
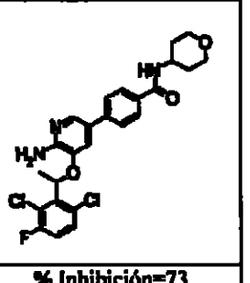
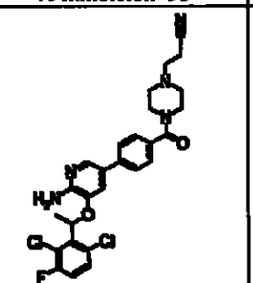
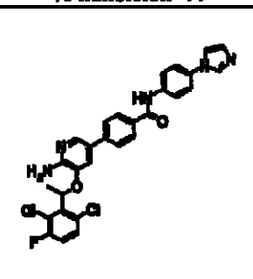
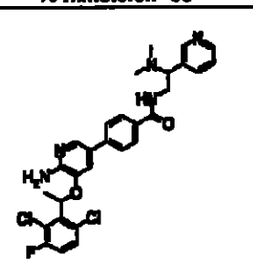
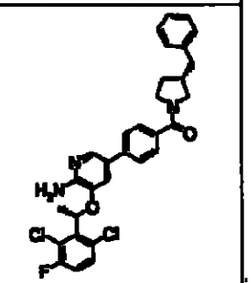
5

Sección I: Ejemplos L- 129 a L- 144

			
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% Inhibición=68	% Inhibición=76	% Inhibición=76	% Inhibición=61
			
% Inhibición=78	% Inhibición=83	% Inhibición=60	% Inhibición=64
			
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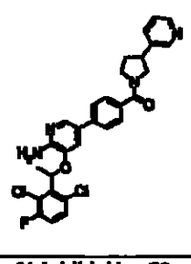
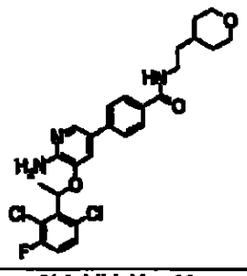
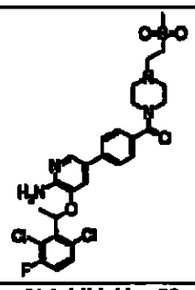
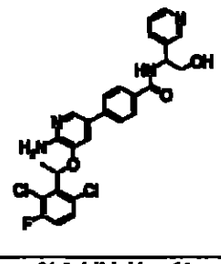
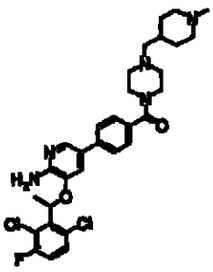
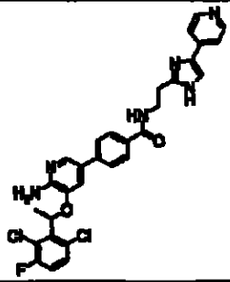
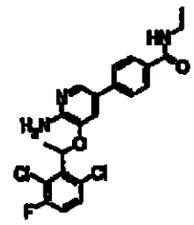
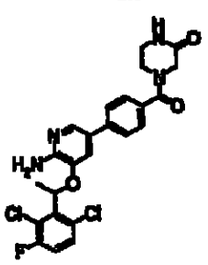
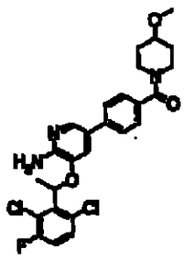
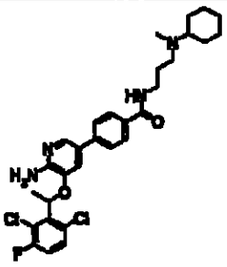
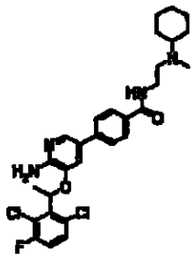
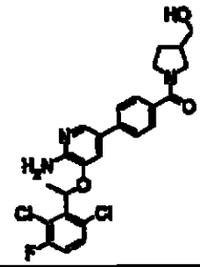
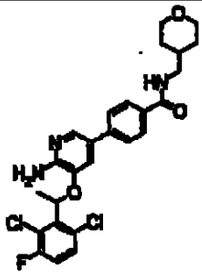
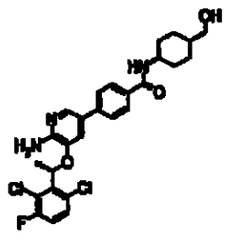
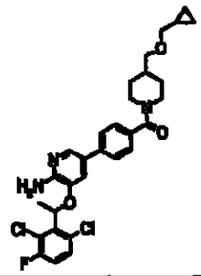
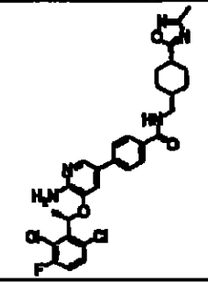
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Sección J: Ejemplos L- 145 a L- 160

			
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% Inhibición=70	% Inhibición=81	% Inhibición=58	% Inhibición=53
			
% Inhibición=95	% Inhibición=77	% Inhibición=66	% Inhibición=73
			
% Inhibición=77	% Inhibición=63	% Inhibición=78	% Inhibición=59

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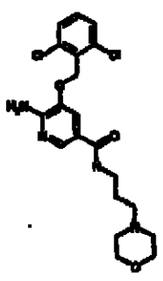
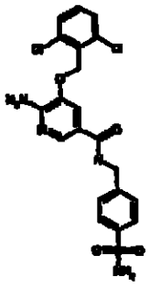
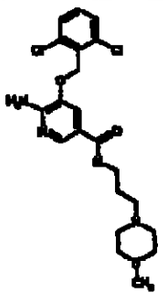
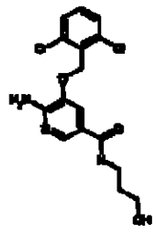
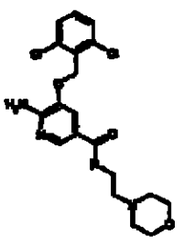
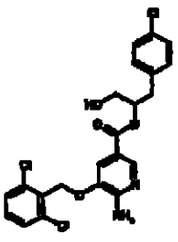
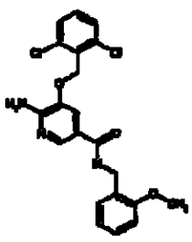
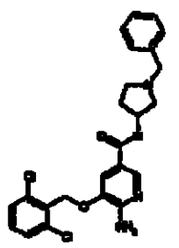
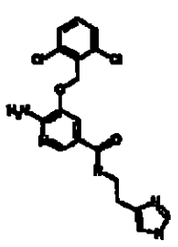
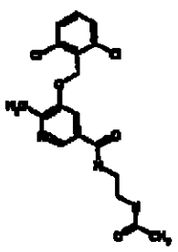
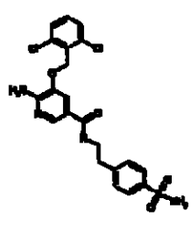
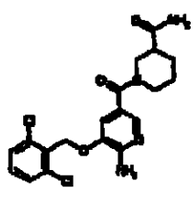
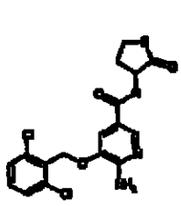
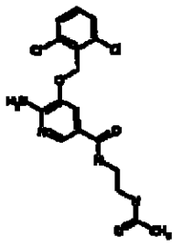
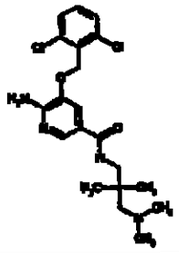
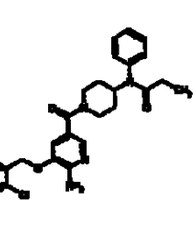
Sección K: Ejemplos L- 161 a L- 176

			
% Inhibición=79	% Inhibición=66	% Inhibición=83	% Inhibición=61
			
% Inhibición=88	% Inhibición=67	% Inhibición=66	% Inhibición=90
			
% Inhibición=79	% Inhibición=77	% Inhibición=69	% Inhibición=79
			
% Inhibición=63	% Inhibición=68	% Inhibición=60	% Inhibición=51

5

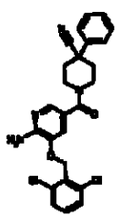
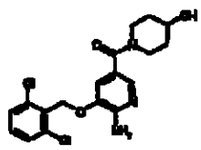
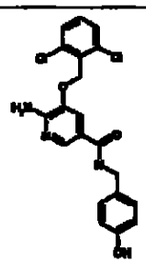
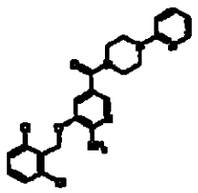
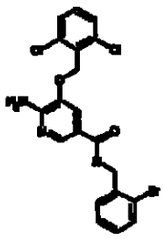
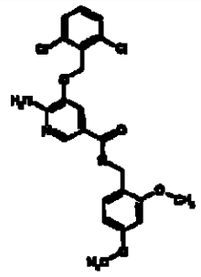
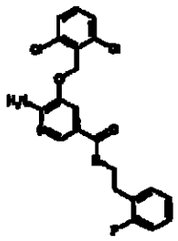
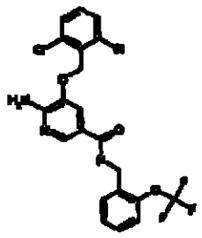
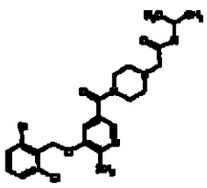
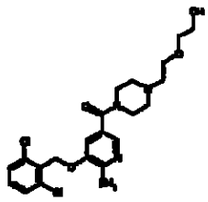
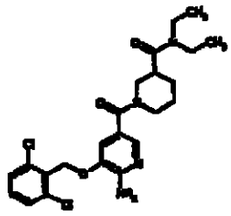
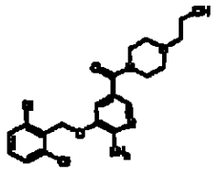
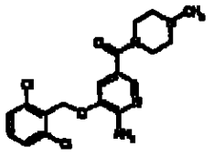
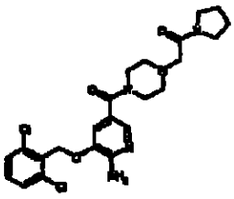
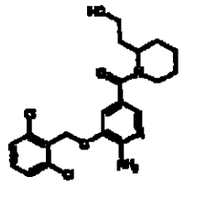
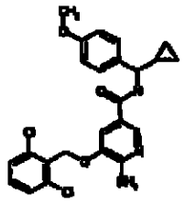
Tabla 6

Sección A: Ejemplos L- 177 a L- 192

			
% Inhibición=26	% Inhibición=30	% Inhibición=24	% Inhibición=26
			
% Inhibición=31	% Inhibición=27	% Inhibición=32	% Inhibición=27
			
% Inhibición=29	% Inhibición=30	% Inhibición=30	% Inhibición=39
			
% Inhibición=35	% Inhibición=35	% Inhibición=38	% Inhibición=44

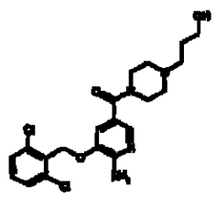
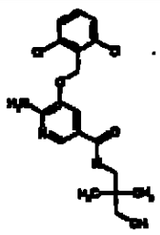
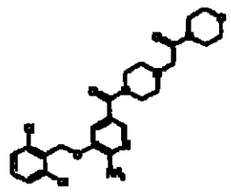
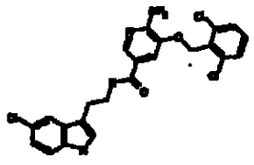
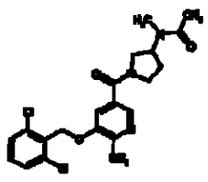
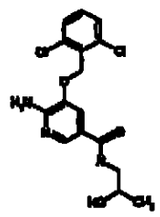
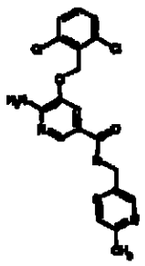
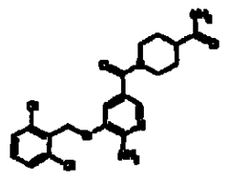
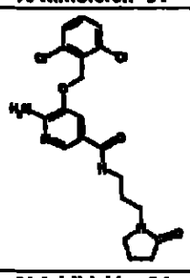
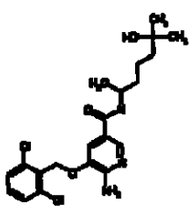
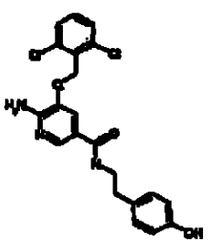
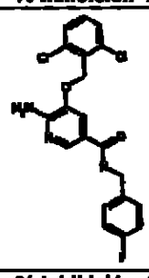
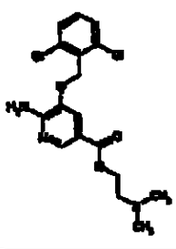
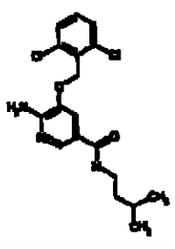
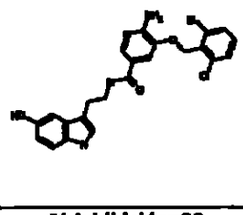
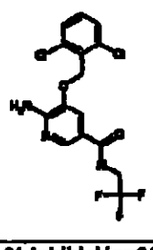
5

Sección B: Ejemplos L- 193 a L- 208

			
% Inhibición=37	% Inhibición=35	% Inhibición=37	% Inhibición=34
			
% Inhibición=36	% Inhibición=59	% Inhibición=33	% Inhibición=31
			
% Inhibición=30	% Inhibición=33	% Inhibición=33	% Inhibición=51
			
% Inhibición=32	% Inhibición=32	% Inhibición=33	% Inhibición=27

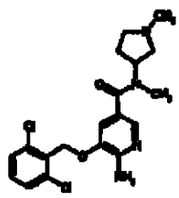
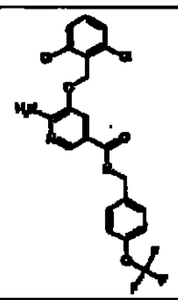
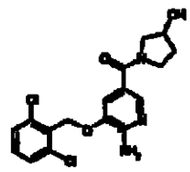
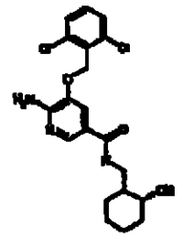
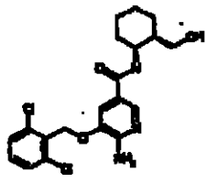
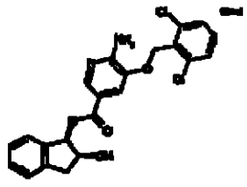
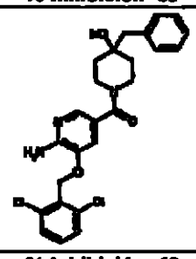
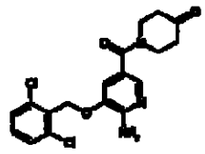
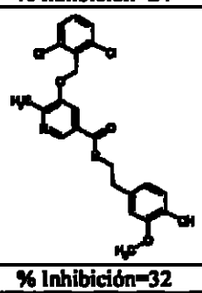
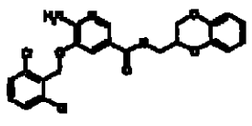
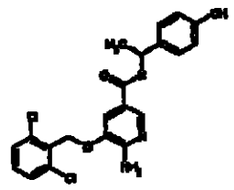
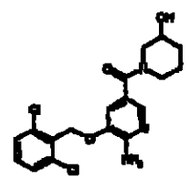
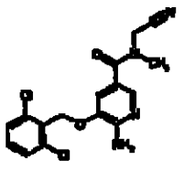
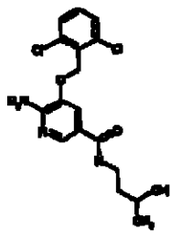
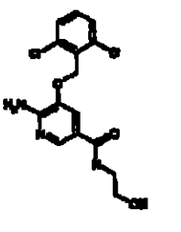
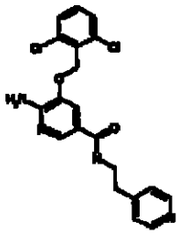
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Sección C: Ejemplos L- 209 a L- 224

			
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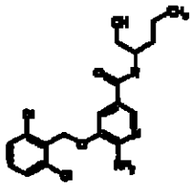
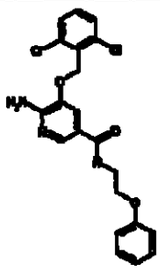
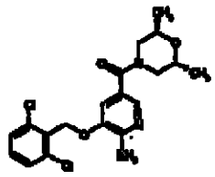
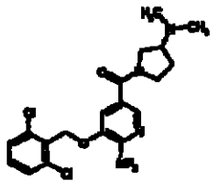
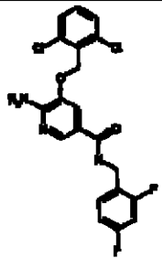
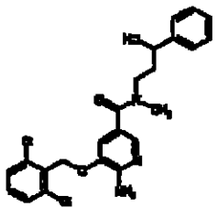
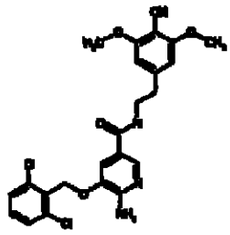
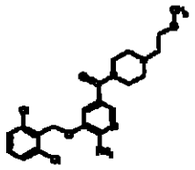
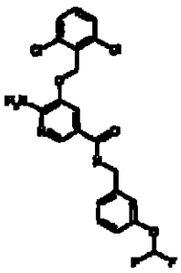
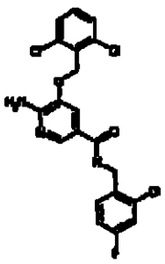
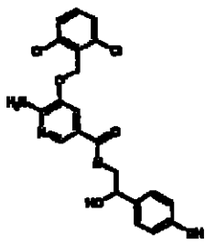
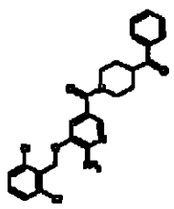
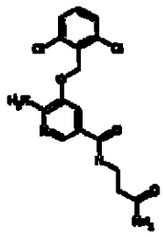
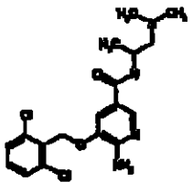
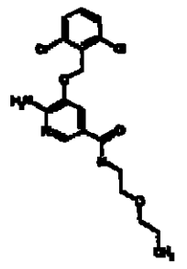
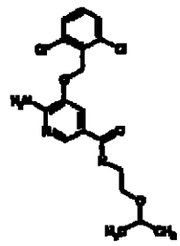
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Sección D: Ejemplos L- 225 a L- 240

			
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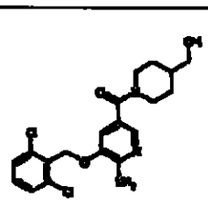
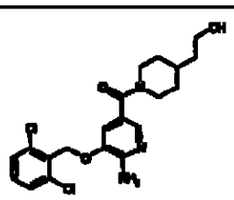
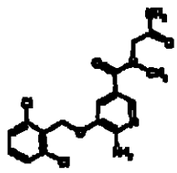
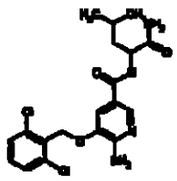
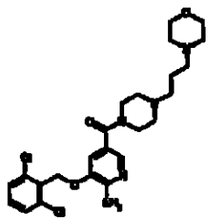
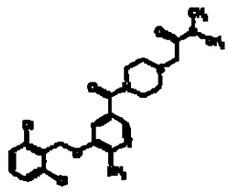
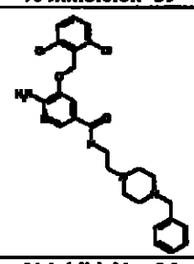
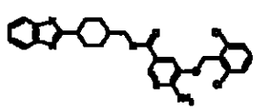
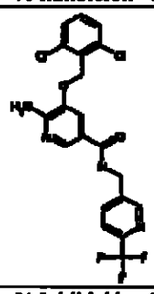
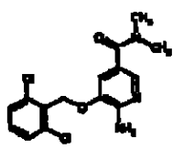
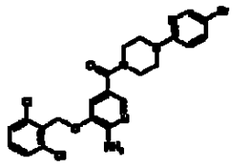
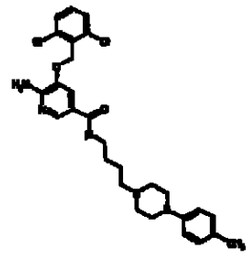
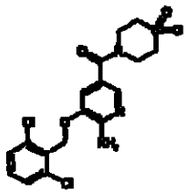
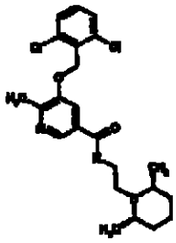
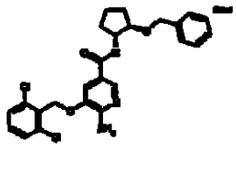
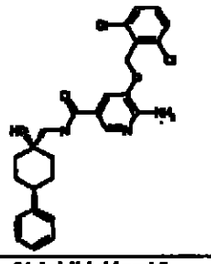
Sección E: Ejemplos L- 241 a L- 256

			
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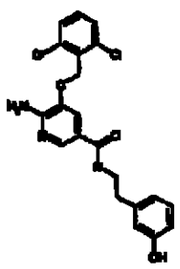
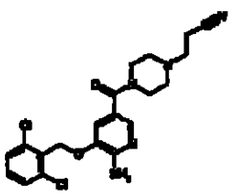
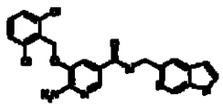
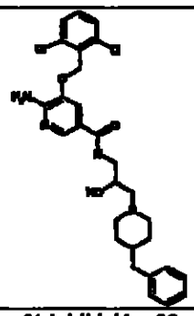
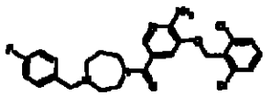
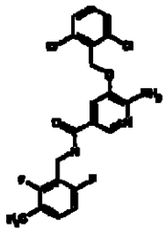
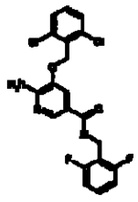
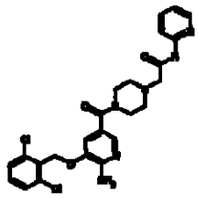
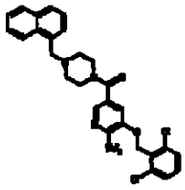
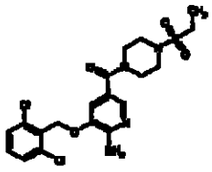
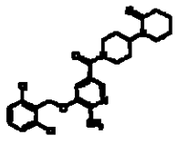
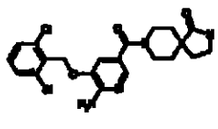
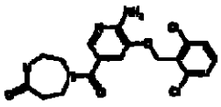
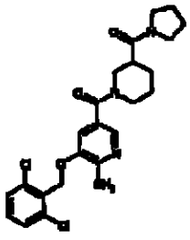
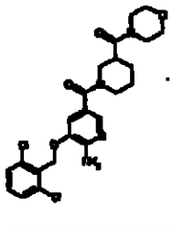
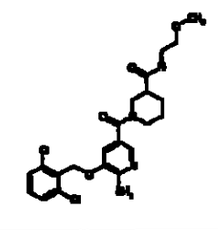
503

Sección F: Ejemplos L- 257 a L- 272

			
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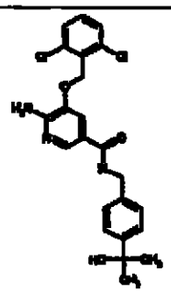
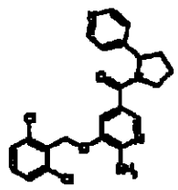
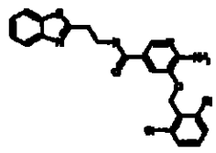
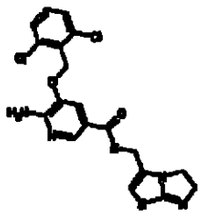
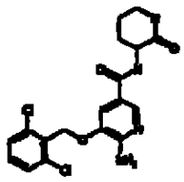
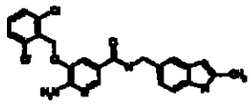
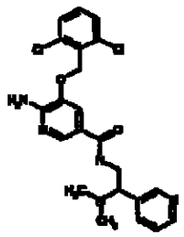
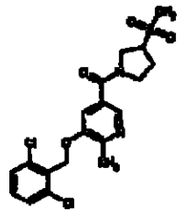
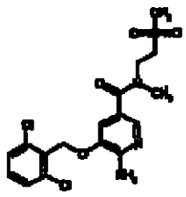
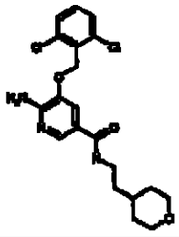
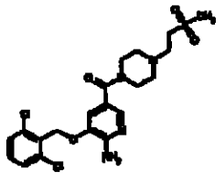
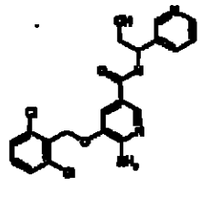
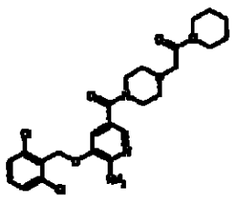
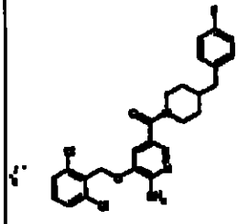
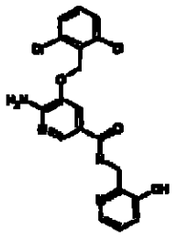
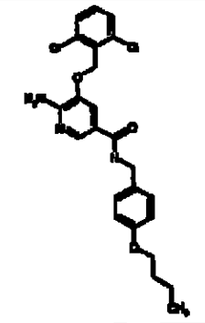
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Sección G: Ejemplos L- 273 a L- 288

			
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% Inhibición=26	% Inhibición=31	% Inhibición=32	% Inhibición=56
			
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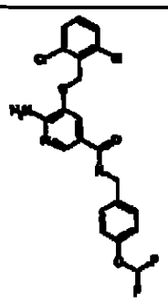
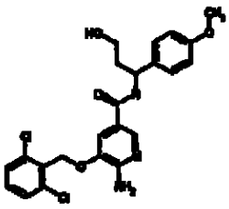
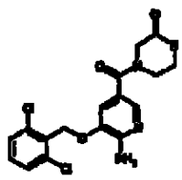
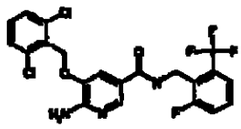
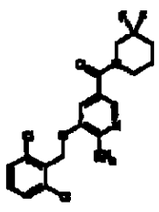
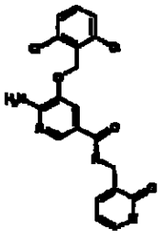
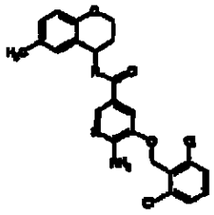
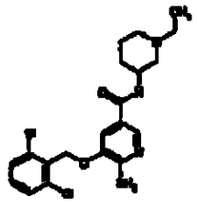
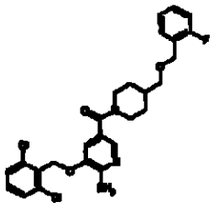
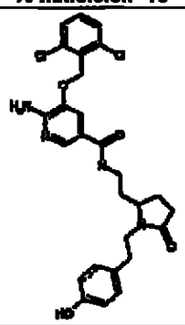
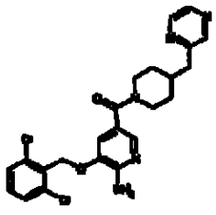
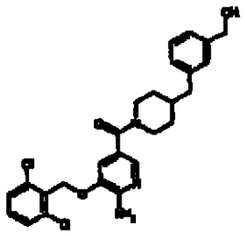
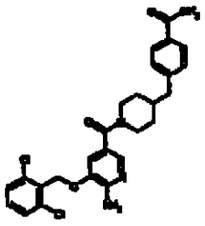
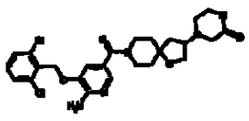
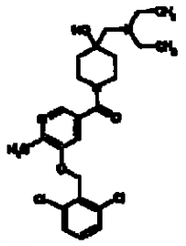
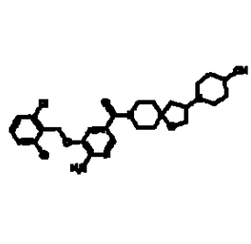
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Sección G: Ejemplos L- 289 a L- 304

			
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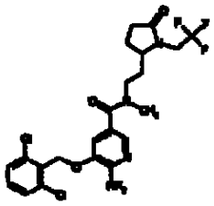
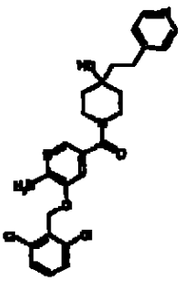
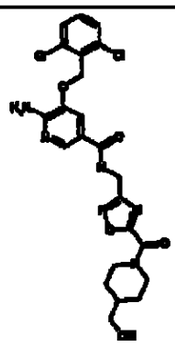
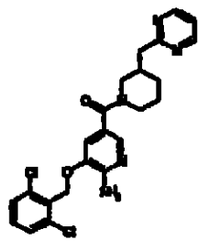
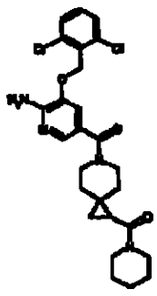
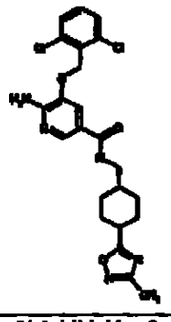
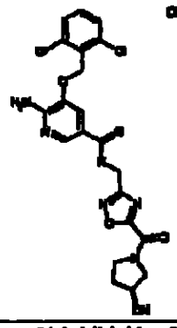
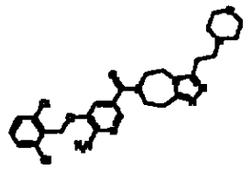
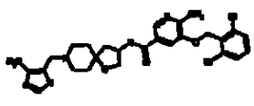
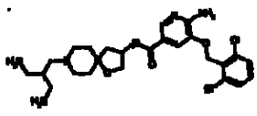
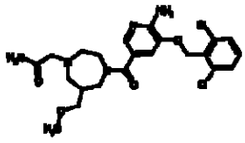
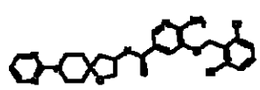
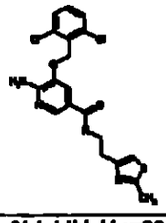
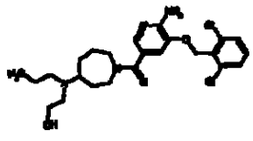
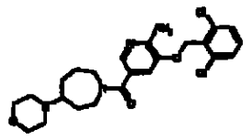
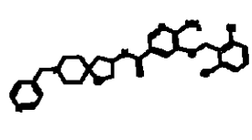
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Sección I: Ejemplos L- 305 a L- 320

			
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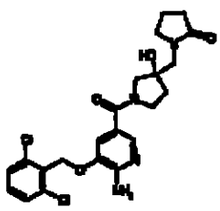
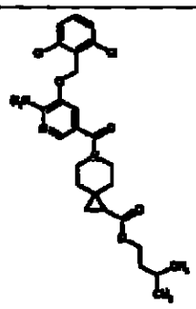
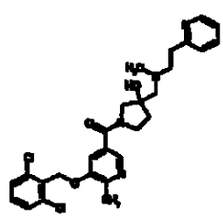
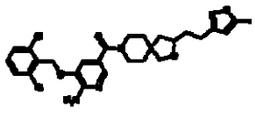
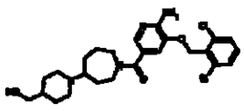
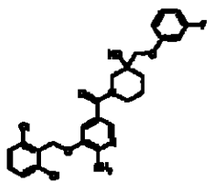
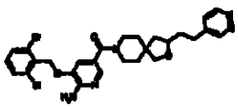
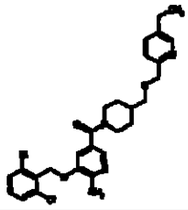
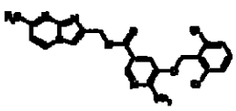
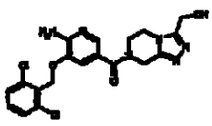
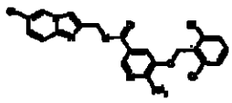
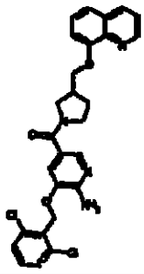
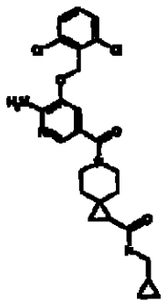
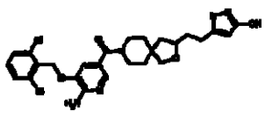
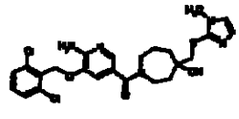
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Sección J: Ejemplos L- 321 a L- 336

			
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% Inhibición=26	% Inhibición=3	% Inhibición=26	% Inhibición=27
			
% Inhibición=30	% Inhibición=74	% Inhibición=23	% Inhibición=21
			
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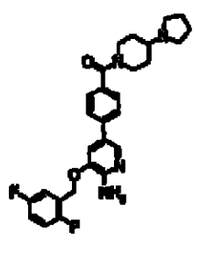
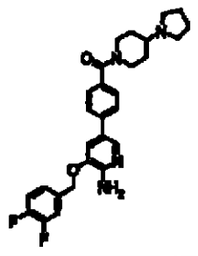
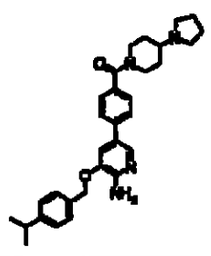
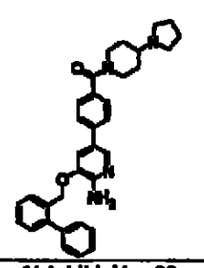
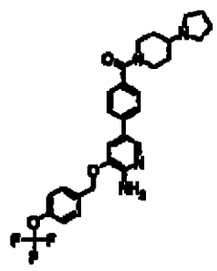
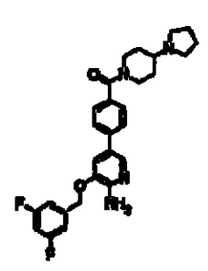
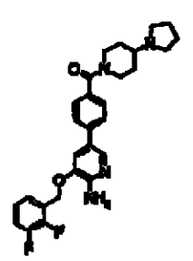
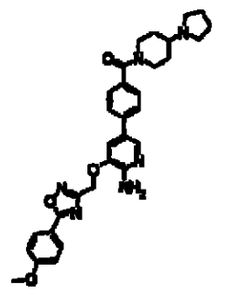
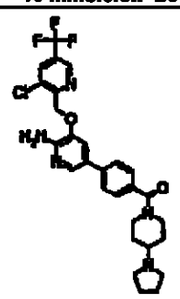
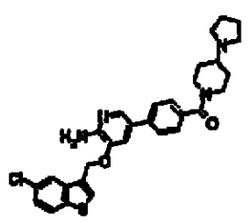
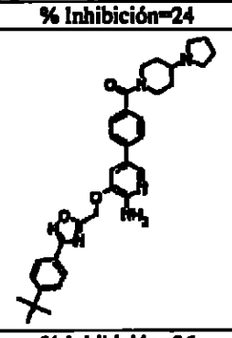
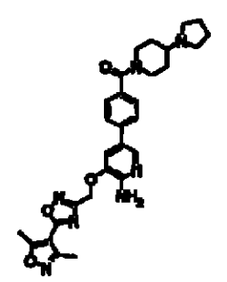
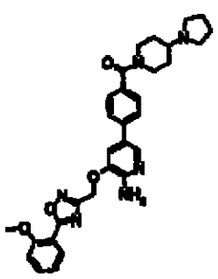
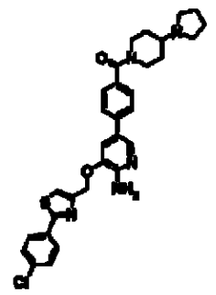
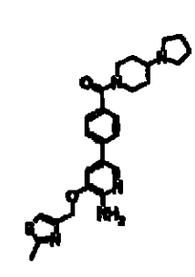
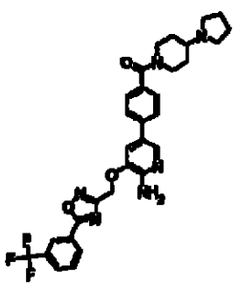
Sección K: Ejemplos L- 337 a L- 352

			
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% Inhibición=20	% Inhibición=36	% Inhibición=37	% Inhibición=41
			
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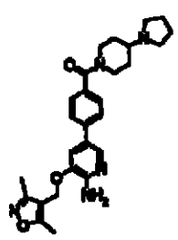
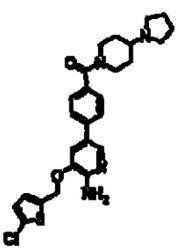
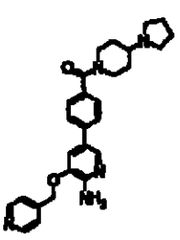
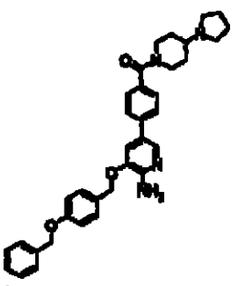
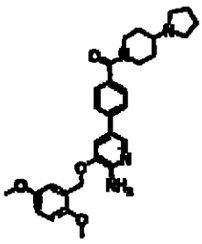
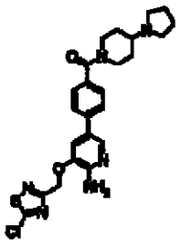
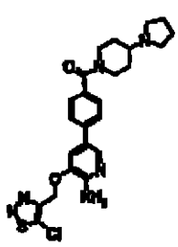
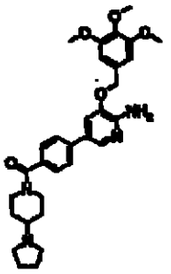
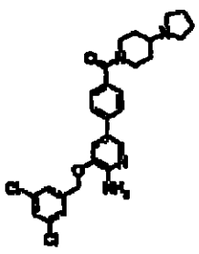
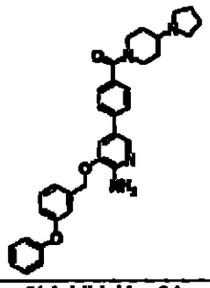
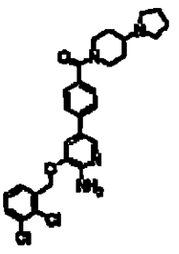
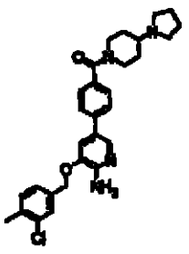
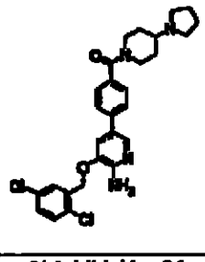
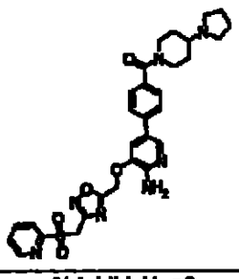
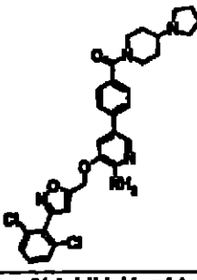
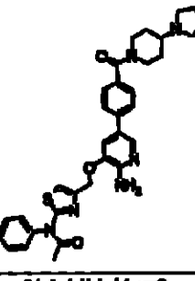
Tabla 7

Sección A: Ejemplos L- 353 a L- 368

			
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% Inhibición=8	% Inhibición=37	% Inhibición=36	% Inhibición=6
			
% Inhibición=8	% Inhibición=9	% Inhibición=6	% Inhibición=27

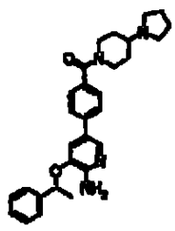
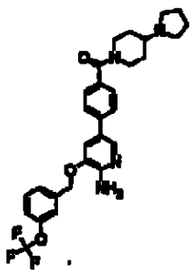
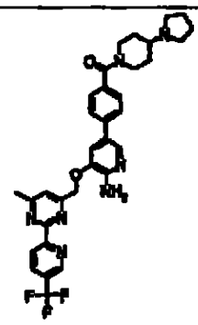
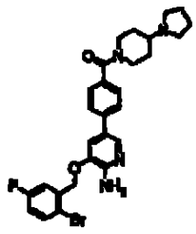
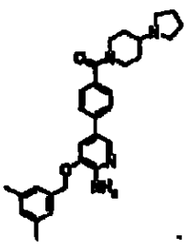
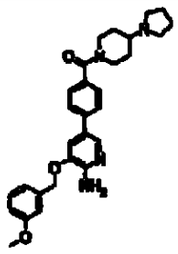
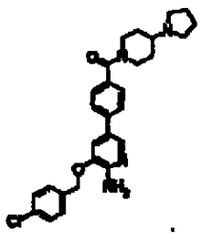
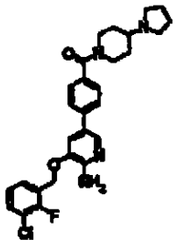
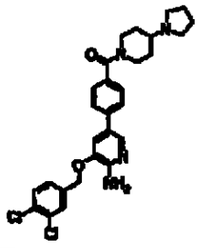
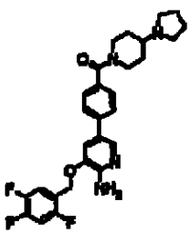
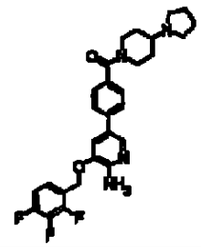
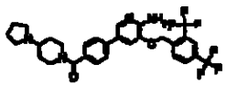
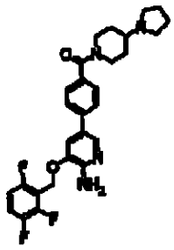
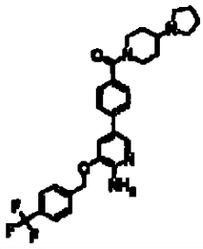
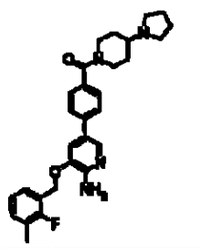
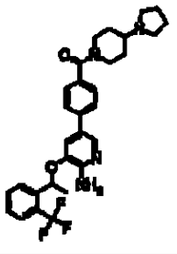
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Sección B: Ejemplos L- 369 a L- 384

			
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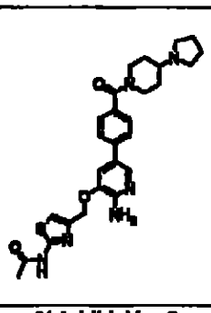
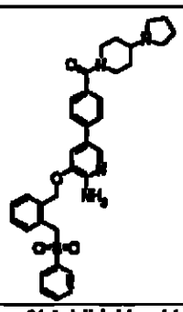
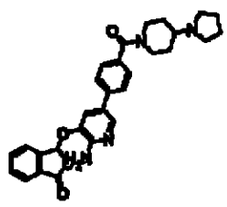
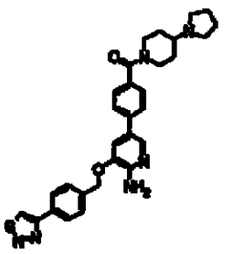
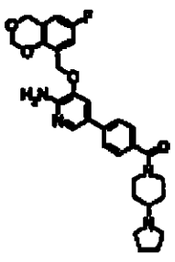
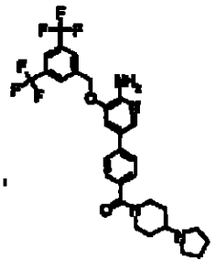
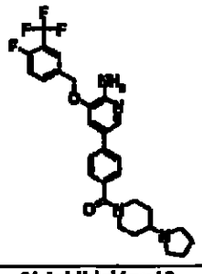
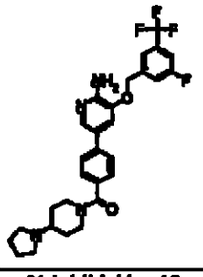
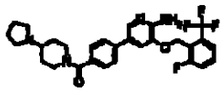
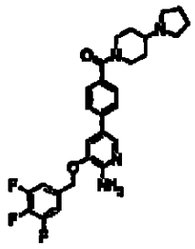
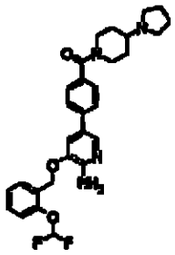
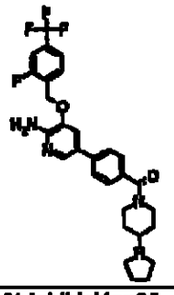
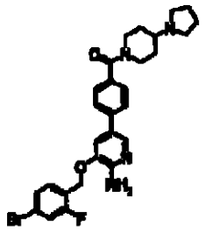
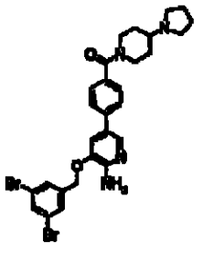
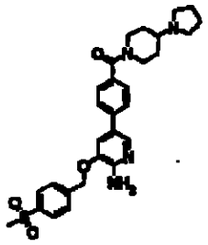
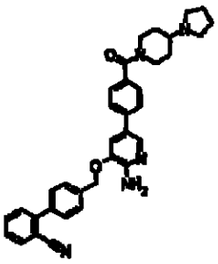
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Sección C: Ejemplos L- 385 a L- 400

			
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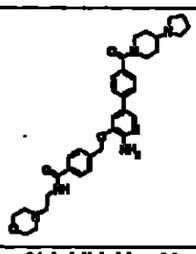
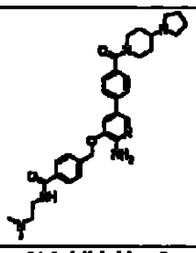
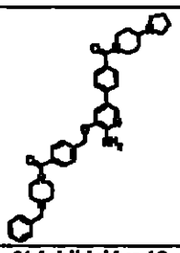
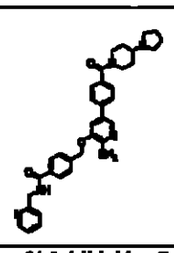
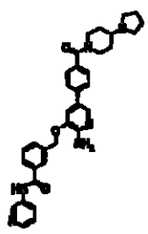
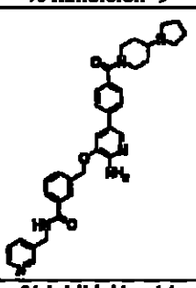
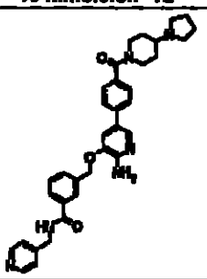
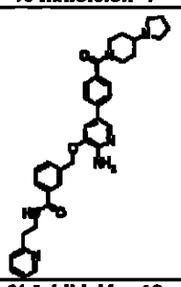
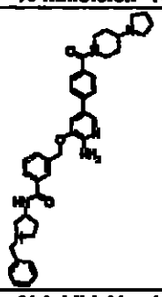
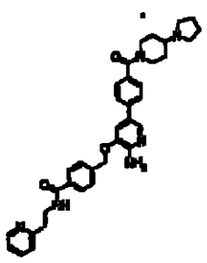
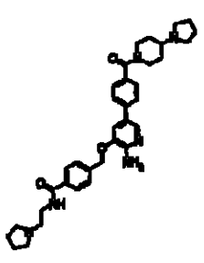
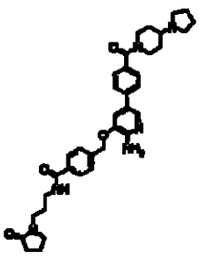
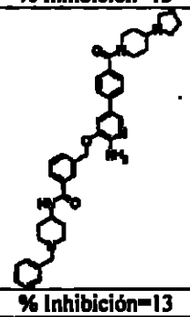
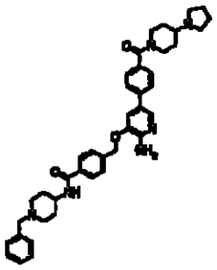
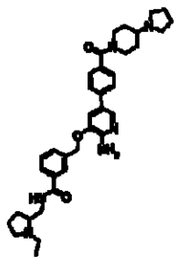
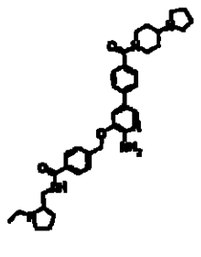
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Sección D: Ejemplos L- 400 a L- 416

			
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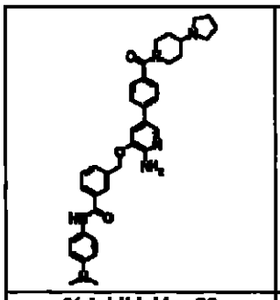
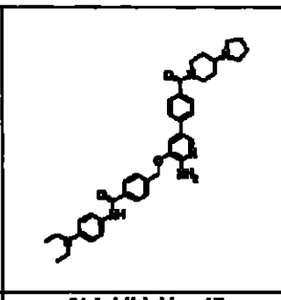
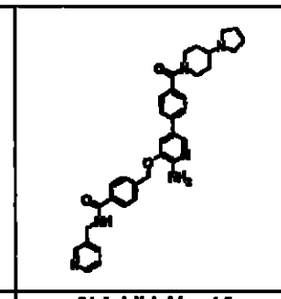
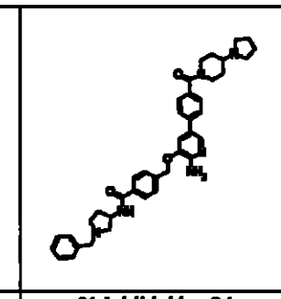
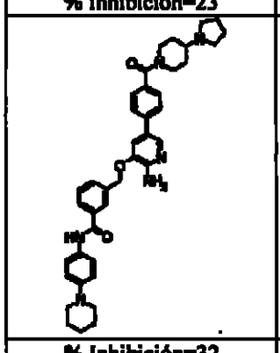
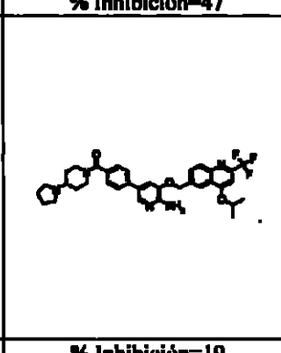
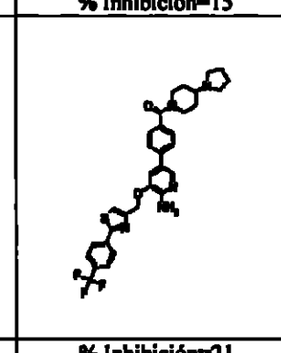
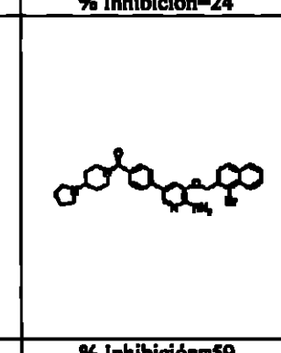
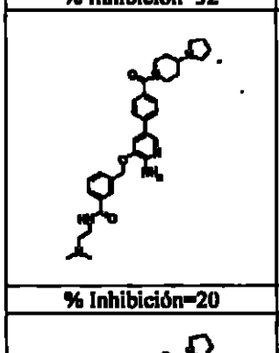
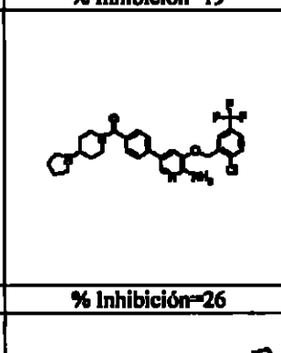
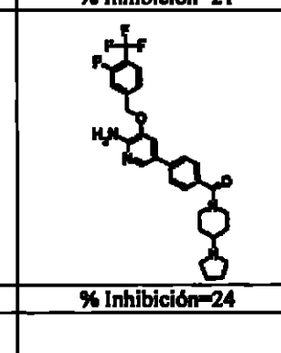
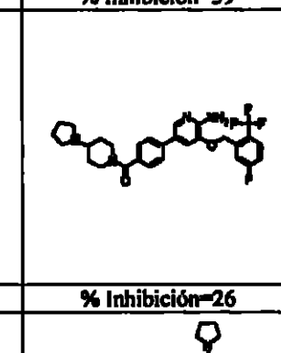
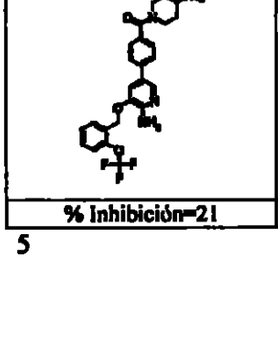
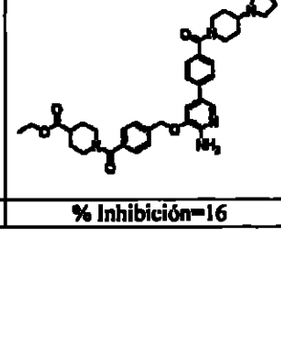
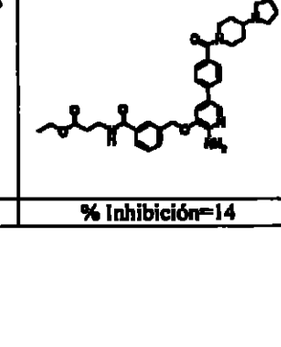
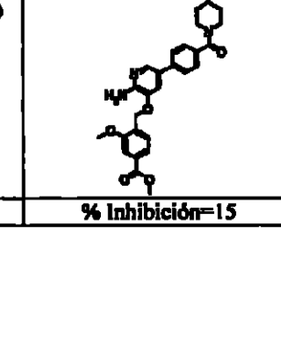
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Sección E: Ejemplos L- 417 a L- 432

			
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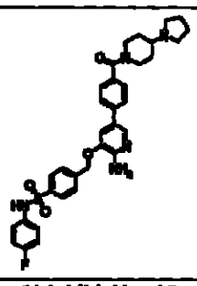
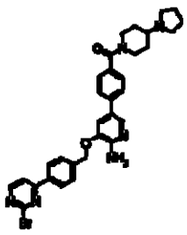
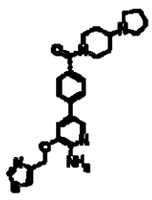
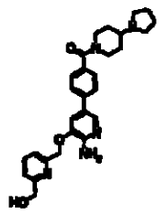
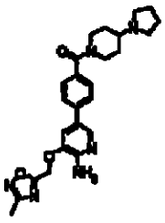
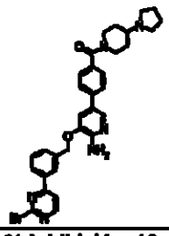
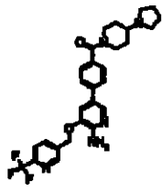
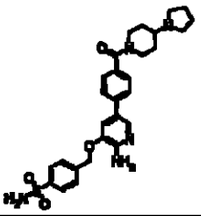
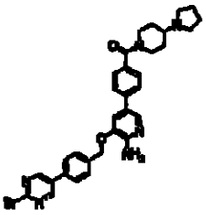
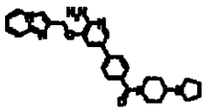
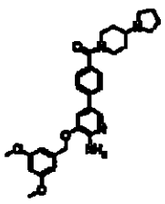
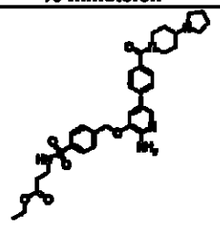
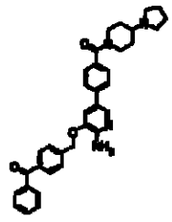
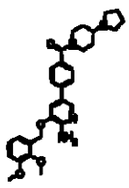
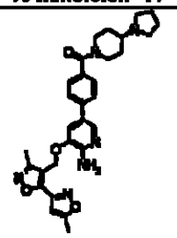
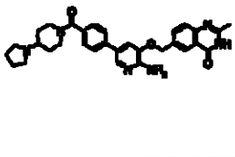
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Sección F: Ejemplos L- 433 a L- 448

			
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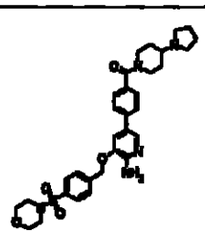
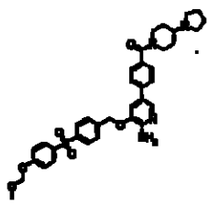
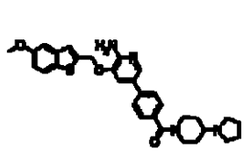
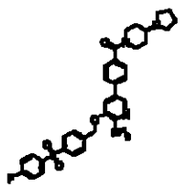
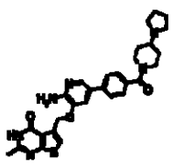
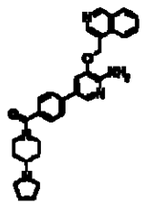
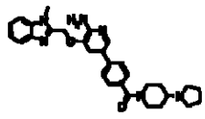
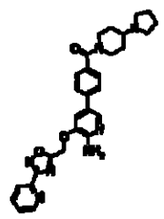
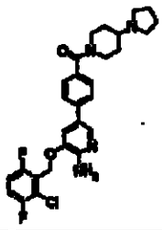
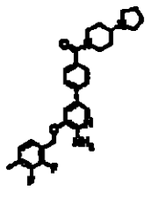
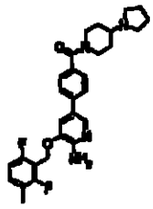
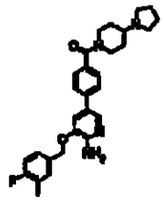
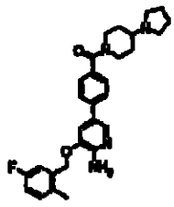
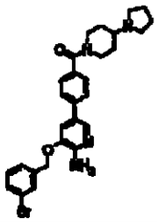
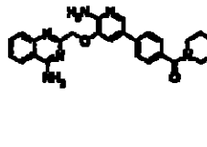
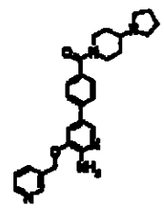
Sección A: Ejemplos L- 449 a L- 464

			
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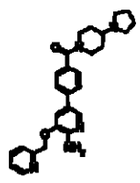
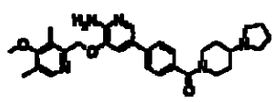
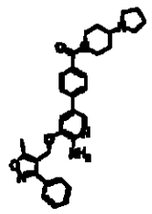
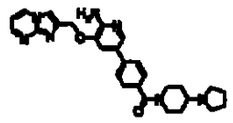
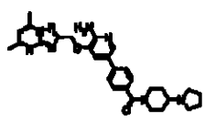
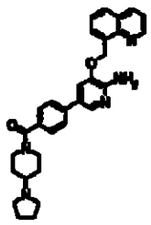
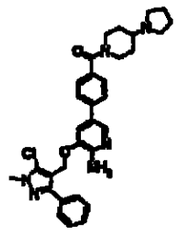
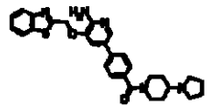
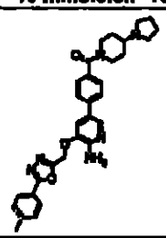
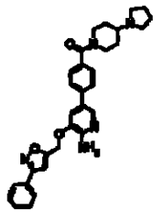
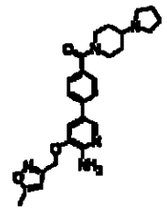
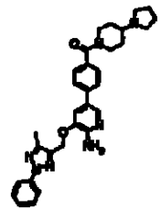
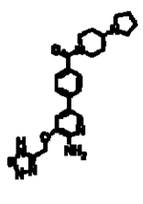
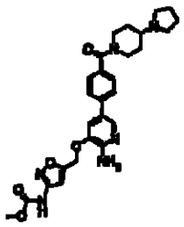
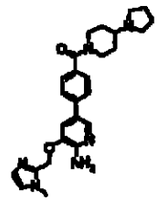
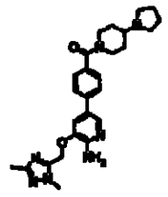
516

Sección H: Ejemplos L- 465 a L- 480

			
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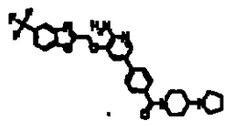
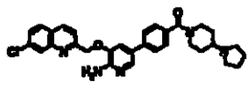
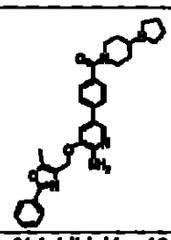
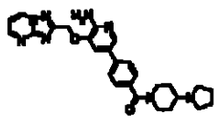
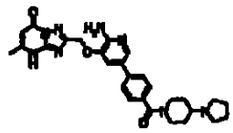
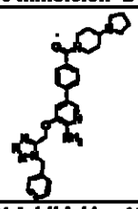
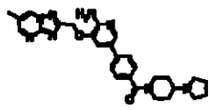
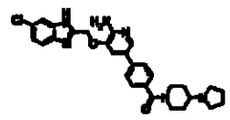
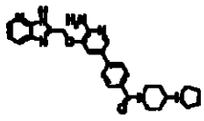
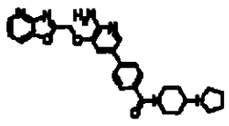
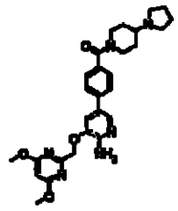
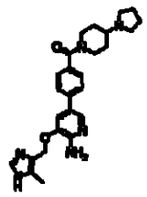
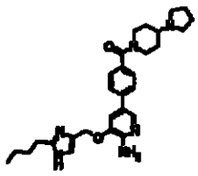
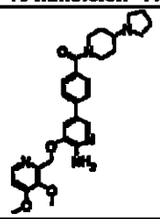
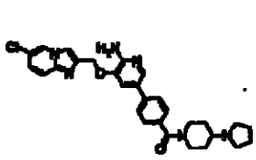
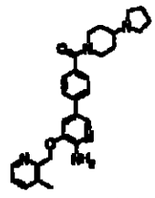
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Sección I: Ejemplos L- 481 a L- 496

			
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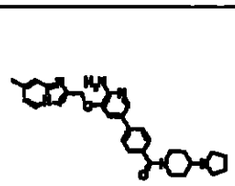
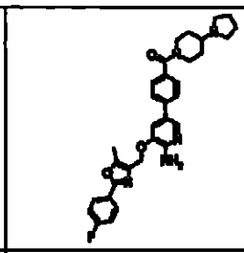
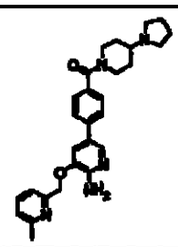
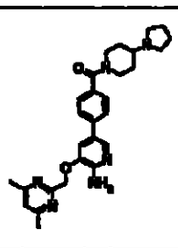
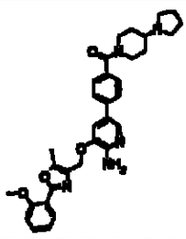
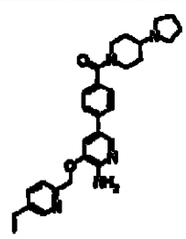
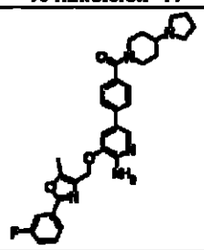
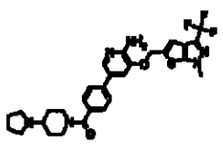
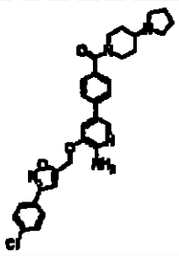
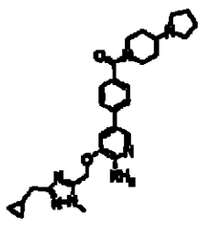
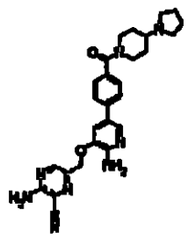
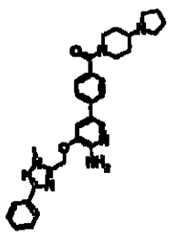
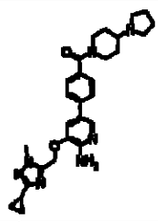
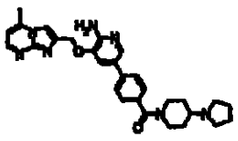
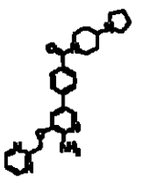
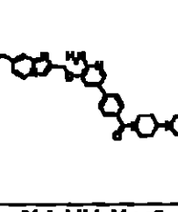
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Sección J: Ejemplos L- 497 a L- 512

			
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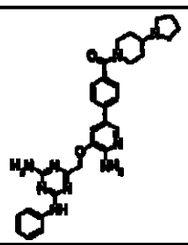
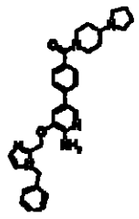
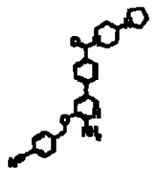
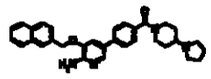
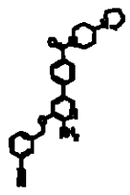
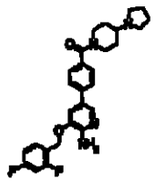
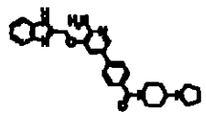
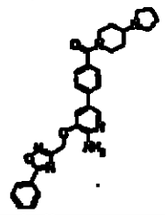
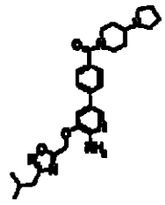
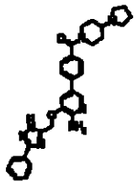
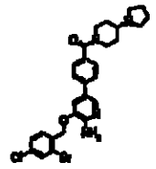
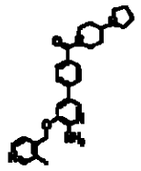
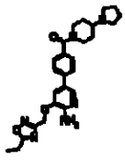
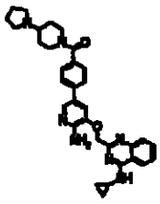
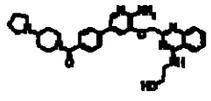
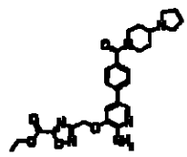
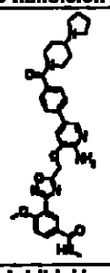
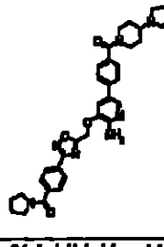
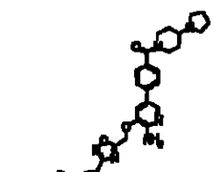
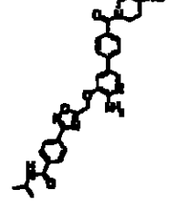
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Sección K: Ejemplos L- 513 a L- 528

			
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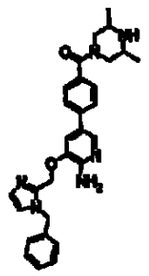
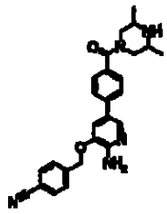
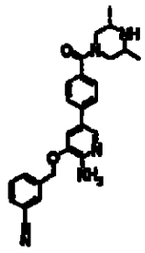
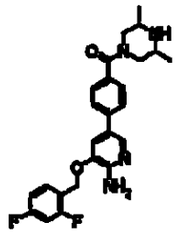
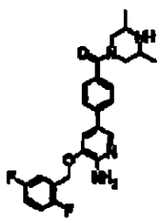
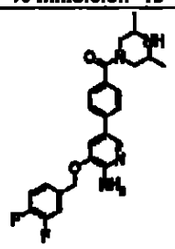
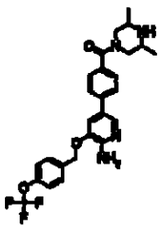
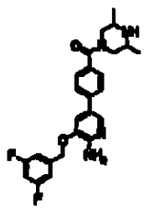
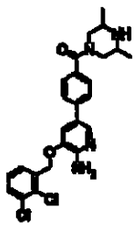
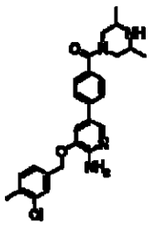
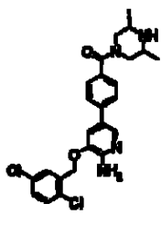
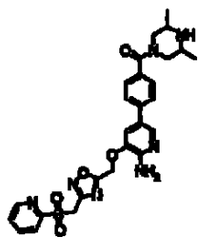
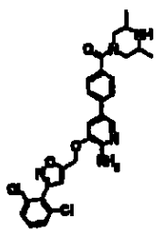
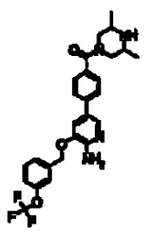
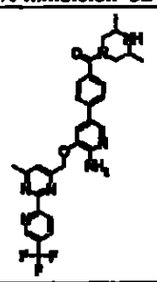
Sección L: Ejemplos L- 1529 a L- 548

			
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% Inhibición=11	% Inhibición=11	% Inhibición=64	% Inhibición=18

5

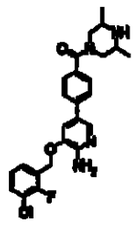
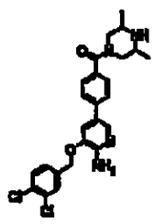
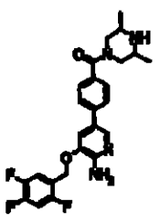
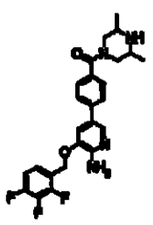
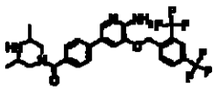
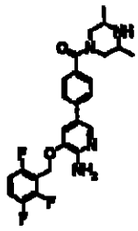
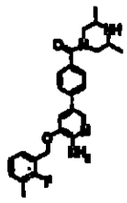
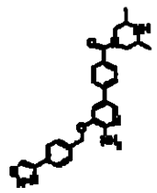
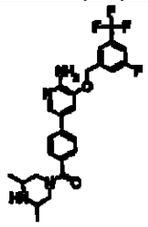
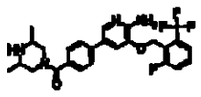
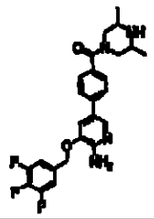
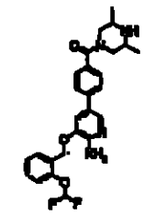
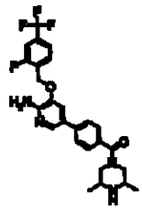
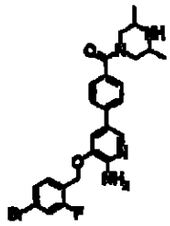
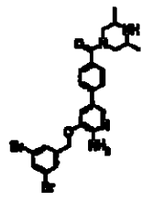
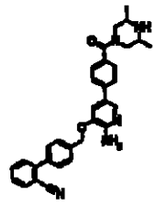
Tabla 8

Sección A: Ejemplos L- 549 a L- 561

			
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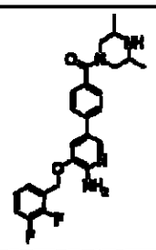
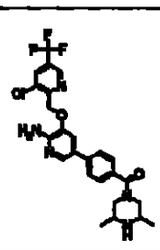
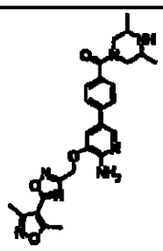
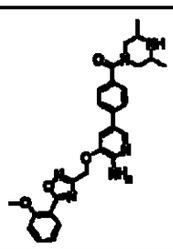
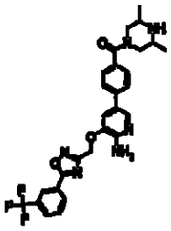
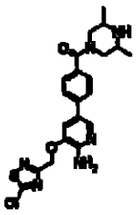
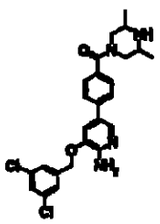
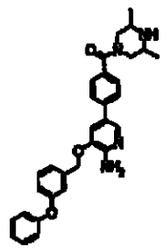
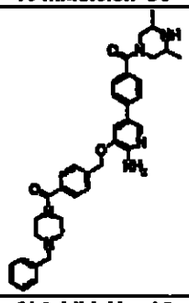
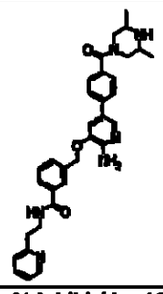
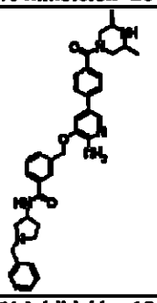
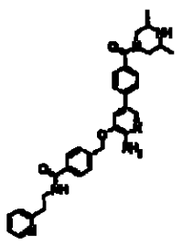
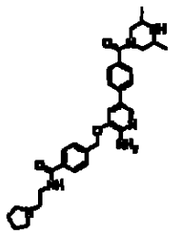
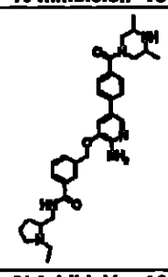
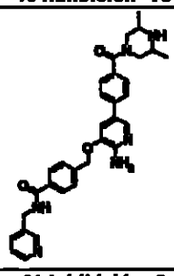
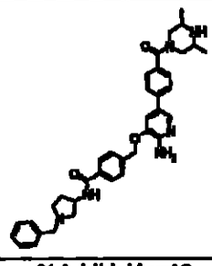
5

Sección B: Ejemplos L- 565 a L- 580

			
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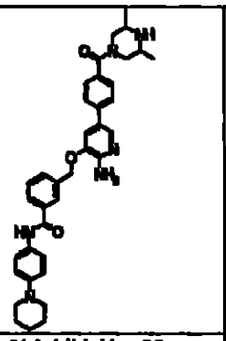
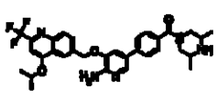
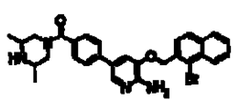
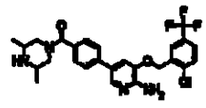
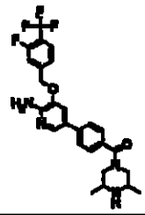
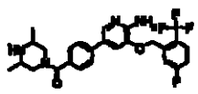
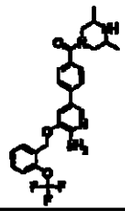
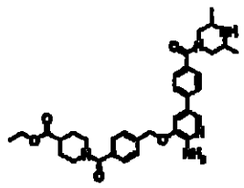
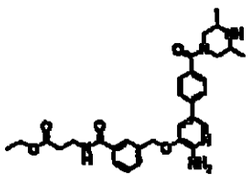
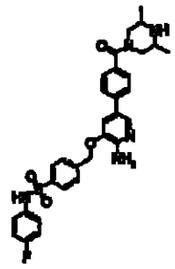
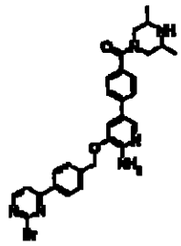
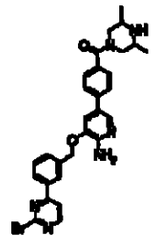
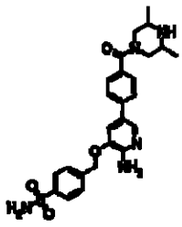
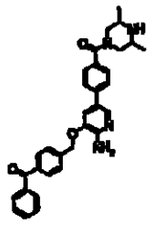
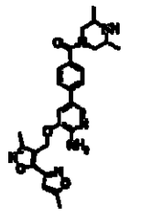
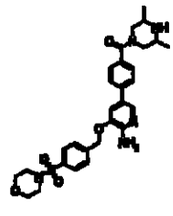
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Sección C: Ejemplos L- 581 a L- 596

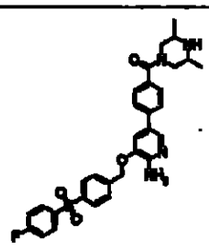
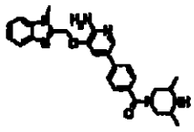
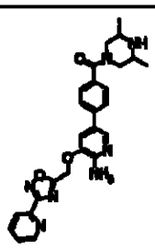
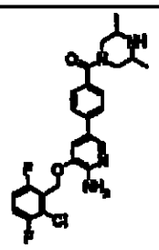
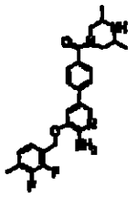
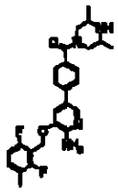
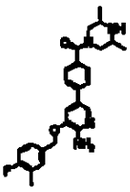
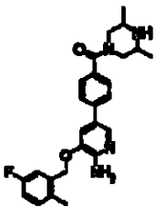
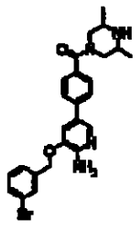
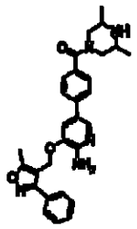
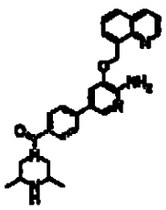
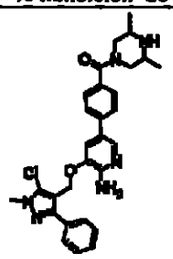
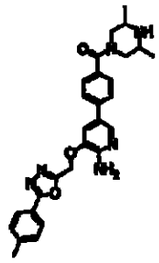
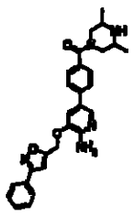
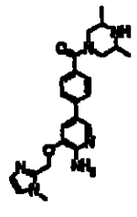
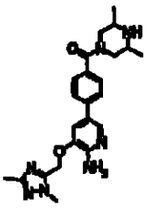
			
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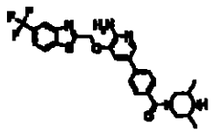
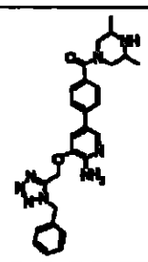
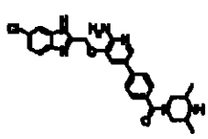
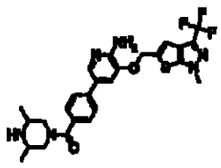
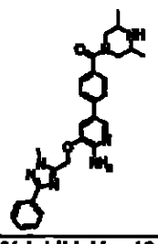
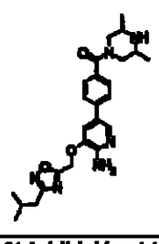
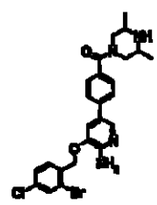
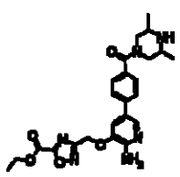
Sección D: Ejemplos L- 597 a L- 612

			
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Sección E: Ejemplos L- 613 a L- 628

			
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Sección F: Ejemplos L- 629 a L- 636

			
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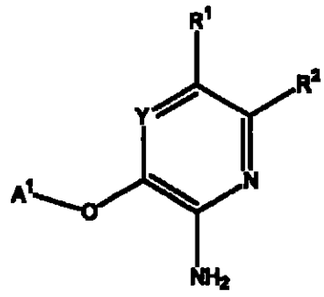
El presente invento no está limitado en alcance por los aspectos ejemplificados que pretenden ilustrar aspectos únicos del invento, y cualquier clon, secuencias de ADN o aminoácidos que son funcionalmente equivalentes están dentro del alcance del invento. En realidad, las diferentes modificaciones del invento además de aquellas descritas en la presente serán manifiestas para aquellos con experiencia en el estado de la técnica a partir de la anterior descripción e ilustraciones anexas. Tales modificaciones pretenden caer dentro del alcance de las reivindicaciones anexas.

La divulgación de la Solicitud Provisional Americana No. 60/449.588, registrada en Febrero 26 de 2003, y Solicitud Provisión Americana U.S. No. 60/540.229, registradas en Enero 29 de 2004, son incorporadas en la presente como referencia en su totalidad

Todas las referencias citadas en la presente son incorporadas como referencia en su totalidad.

REIVINDICACIONES

1. Un compuesto de la formula 1



1

en donde:

Y es N o CR^{12}:

R1 es seleccionado de arilo C6- 12, heterarilo de 5- 12 miembros, cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, - O(CR6R7)nR4, - C(O)R4, - C(O)OR4, - CN, - NO2, - S(O)mR4, - SO2NR4R5, - C(O)NR4R5, - NR4(C(O)R5, - C(=NR6)NR4R5, alquilo C1- 8, alquenilo C2- 8, y alquinilo C2- 8; y cada hidrógeno en R1 es opcionalmente substituido por uno o más grupos R3;

R2 es hidrogeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5, y cada hidrógeno en R2 es opcionalmente sustituido por uno o más grupos R8;

R3 es halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5, cada hidrógeno en R3 es opcionalmente sustituido por uno o más grupos R8, y grupos los R3 sobre átomos adyacentes se pueden combinar para formar un arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o grupo heteroalicíclico de 3- 12 miembros;

Cada uno de R4, R5, R6 y R7 es independientemente hidrógeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de nitrógeno pueden junto con el nitrógeno al cual están unidos ser combinados para formar un heteroalicíclico de 13 a 12 miembros o grupo heteroarilo de 5- 12 miembros opcionalmente conteniendo de 1 a 3 heteroátomos adicionales seleccionados de N. O y S; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de carbono puede ser combinados para formar un cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, o grupo heteroarilo de 5- 12 miembros; y cada hidrógeno en R4, R5, R6 y R7 es opcionalmente sustituido por uno o más grupos R8;

cada R8 es independientemente halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5 - 12 miembros, - CN, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O- (CH2)n(heteroalicíclico de 3- 12 miembros) o - O- (CH2)n(heteroarilo de 5- 12 miembros); y cada hidrógeno en R8 es opcionalmente sustituido por uno o más grupos R11;

A1 es - (CR9R10)n- A2 excepto que:

(i) cuando Y es N y R1 es arilo sustituido o no sustituido o heteroarilo sustituido o no sustituido, A1 es - (CR9R10)n- A2 y n no es cero; y

(ii) cuando Y es N y R2 es H y A1 es m- clorobencilo, R1 es piperazina no sustituida;

cada R9 y R10 es independientemente hidrógeno, halógeno, alquilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5; R9 y R10 se pueden combinar para formar un cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, arilo C6- 12 o anillo de heteroarilo de 5- 12 miembros; y cada hidrógeno en R9 y R10 es opcionalmente sustituido por uno o más grupos R3;

A2 es arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o heteroalicíclico de 3 - 12 miembros, y A2 es opcionalmente sustituido por uno o más grupos R3;

530

cada R11 es indcpendientemente halógeno, alquilo C1- 12, alcoxilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5- 12 miembros, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O_(CH2)n(heteroalicíclico de 3- 12 miembros), - O- (CH2)n(heteroarilo de 5- 12 miembros) o - CN, y cada hidrógeno en R11 es un generalmente sustituido por uno o más grupos seleccionados de halógeno - OH, - CN, alquilo C1- 12, el cual puede ser parcial o totalmente halogenado, alquilo - O- C1- 12 el cual puede ser total o parcialmente halogenado, - CO, - SO y - SO2;

R12 es hidrógeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5 y cada hidrogeno en R12 es opcionalmente sustituido por uno o más grupos R3;

R1 y R2 o R1 y R2 se pueden combinar juntos para formar arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12, o grupo heteroalicíclico de 3- 12 miembros;

m es 0, 1 o 2;

n es 0, 1, 2, 3 o 4; y

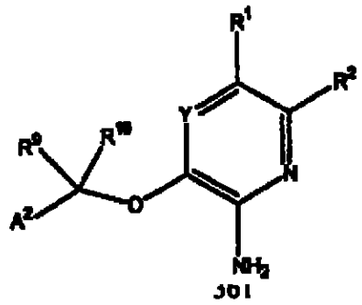
p es 1 o 2;

o una sal, solvato o hidrato farmaceuticamente aceptable del mismo.

2. El compuesto de la reivindicación 1, en donde Y es N.

3. El compuesto de la reivindicación 1, en donde Y es CR^{12}.

4. El compuesto de la reivindicación 1, en donde el compuesto tiene la formula 1a



1a

en donde A2 es arilo C6- 12 o heteroarilo de 5- 12 miembros opcionalmente sustituido por uno o más grupos R^3.

5. El compuesto de la reivindicación 4, en donde R1 es seleccionado del arilo C6- 12 y y heteroarilo de 5- 12 miembros, y cada hidrógeno en R1 es opcionalmente sustituido por uno o mas grupos R3.

6. El compuesto de la reivindicación en donde R1 es seleccionado de cicloalquilo C3- 12, heteroaliciclico de 3- 12 miembros, - O(CR6R7)nR4, - C(O)R4, - C(O)OR4, - CN, - NO2, - S(O=mR4, - SO2NR4R5, - C(O)NR4R5, - NR4C(O)R5, - C(=NR6)NR4R5, alquilo C1- 8, alquenilo C2- 8, y alquinilo C2- 8; y cada hidrógeno en R1 es opcionalmente sustituido por uno o más grupos R3.

7. El compuesto de la reivindicación 4, en donde A2 es sustituido por al menos un átomo de halógeno.

8. El compuesto de la reivindicación 4, en donde R2 es hidrógeno, R9 y R10 son independientemente alquilo C1- 4 y A2 es fenilo sustituido por al menos un átomo de halógeno.

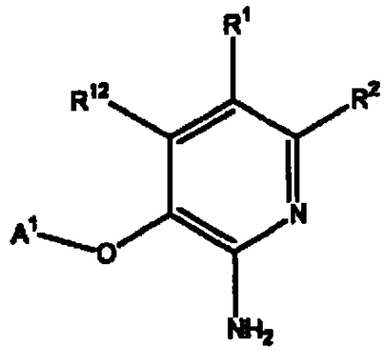
9. El compuesto de la reivindicación 1, en donde R1 es un furano, tiofeno, pirrola, pirrolina, pirrolidina, dioxolano, axazol, imidazol, imidazolina, imidazolidina, pirazol, pirazolina, pirazolidina, isoxazol, isotiazol, oxadiazol, triazol, tiadiazol, pirano, piridina, piperidina, dioxano, morfolina, ditiano, tiomorfolina,g piridazina, pirimidina, pirazina, piperazina, triazina, tritiano o grupo fenilo, y cada hidrógeno en R1 es opcionalmente sustituido por uno o más grupos R3.

10. El compuesto de la reivindicación 1, en donde R1 es un grupo heteroarilo cíclico fusionado, y cada hidrógeno en R1 es opcionalmente sustituido por uno o más grupos R3.

11. El compuesto de la reivindicación 1, en donde R1 es un grupo –SO2NR4R5.

532

12. Un compuesto de la formula 2



2

en donde:

R1 es seleccionado de arilo C6- 12, heterarilo de 5- 12 miembros, cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, - O(CR6R7)nR4, - C(O)R4, - C(O)OR4, - CN, - NO2, - S(O)mR4, - SO2NR4R5, - C(O)NR4R5, - NR4(C(O)R5, - C(=NR6)NR4R5, alquilo C1- 8, alquenilo C2- 8, y alquinilo C2- 8; y cada hidrógeno en R1 es opcionalmente substituido por uno o más grupos R3;

R2 es hidrogeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5, y cada hidrógeno en R2 es opcionalmente sustituido por uno o más grupos R8;

R3 es halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5, cada hidrógeno en R3 es opcionalmente sustituido por uno o más grupos R8, y grupos los R3 sobre átomos adyacentes se pueden combinar para formar un arilo

C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o grupo heteroalicíclico de 3- 12 miembros;

Cada uno de R4, R5, R6 y R7 es independientemente hidrógeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de nitrógeno pueden junto con el nitrógeno al cual están unidos ser combinados para formar un heteroalicíclico de 13 a 12 miembros o grupo heteroarilo de 5- 12 miembros opcionalmente conteniendo de 1 a 3 heteroátomos adicionales seleccionados de N. O y S; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de carbono puede ser combinados para formar un cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, o grupo heteroarilo de 5- 12 miembros; y cada hidrógeno en R4, R5, R6 y R7 es opcionalmente sustituido por uno o más grupos R8;

cada R8 es independientemente halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5 - 12 miembros, - CN, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O- (CH2)n(heteroalicíclico de 3- 12 miembros) o - O- (CH2)n(heteroarilo de 5- 12 miembros); y cada hidrógeno en R8 es opcionalmente sustituido por uno o más grupos R11;

A1 es - (CR9R10)n- A2

cada R9 y R10 es independientemente hidrógeno, halógeno, alquilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5; R9 y R10 se pueden combinar para formar un cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, arilo C6- 12 o anillo de heteroarilo de 5- 12 miembros; y cada hidrógeno en R9 y R10 es opcionalmente sustituido por uno o más grupos R3;

A2 es arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o heteroalicíclico de 3 - 12 miembros, y A2 es opcionalmente sustituido por uno o más grupos R3;

cada R11 es independientemente halógeno, alquilo C1- 12, alcoxilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5- 12 miembros, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O-

(CH2)nC6- 12, - O_(CH2)n(heteroalicíclico de 3- 12 miembros), - O-(CH2)n(heteroarilo de 5- 12 miembros) o - CN, y cada hidrógeno en R11 es un generalmente sustituido por uno o más grupos seleccionados de halógeno - OH, - CN, alquilo C1- 12, el cual puede ser parcial o totalmente halogenado, alquilo - O- C1- 12 el cual puede ser total o parcialmente halogenado, - CO, - SO y - SO2;

R12 es hidrógeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5 y cada hidrogeno en R12 es opcionalmente sustituido por uno o más grupos R3;

R1 y R2 o R1 y R2 se pueden combinar juntos para formar arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12, o grupo heteroalicíclico de 3- 12 miembros;

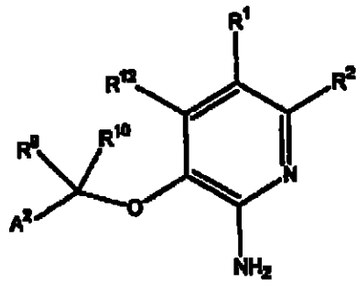
m es 0, 1 o 2;

n es 0, 1, 2, 3 o 4; y

p es 1 o 2;

o una sal, solvato o hidrato farmaceuticamente aceptable del mismo.

13. El compuesto de la reivindicación 12, en donde el compuesto tiene la formula 2a



2a

en donde A2 es arilo C6- 12 o heteroarilo de 5- 12 miembros opcionalmente sustituido por uno o más grupos R3.

14. El compuesto de la reivindicación 13, en donde R1 es seleccionado de arilo C6- 12 y heteroarilo de 5- 12 miembros, y cada hidrógeno en R1 es opcionalmente sustituido por uno o más grupos R3.

15. El compuesto de la reivindicación 13, en donde R1 es seleccionado de cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, - O(CR6R7)nR4, - C(O)R4, - C(O)OR4, - CN, - NO2, - S(O)mR4, - SO2NR4R5, - C(O)NR4R5, NR4C(O)R5, - C(=NR6)NR4R5, alquilo C1- 8, alquenilo C2- 8, y alquinilo C2- 8; y cada hidrógeno en R1 es opcionalmene sustituido por uno o más grupos R3.

16. El compuesto de la reivindicación 13, en donde A2 es sustituido por al menos un átomo de halógeno.

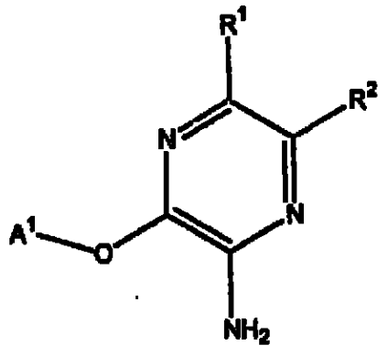
17. El compuesto de la reivindicación 13, en donde R2 es hidrógeno, R9 y R10 son independientemente alquilo C1- 4, y A2 es fenilo sustituido por al menos un átomo de halógeno.

18. El compuesto de la reivindicación 12 en donde R1 es un furano, tiopeno, pirrola, pirrolina, pirrolidina, dioxolano, oxazol, tiazol, imidazolina, imidazolidina, pirazol, pirazolina, pirazolidina, isoxazol, isotiazol, oxadiazol, triazol, tiadiazol, pirano, piridina, piperidina, dioxano, morfolina, ditiano, tiomorfolina, piridazina, pirimidina, pirazina, piperazina, triazina, tritiano, o grupo fenilo, y cada hidrógeno en R1 es opcionalmente sustituido por uno o más grupos R3.

19. El compuesto de la reivindicación 12, en donde R1 es un grupo heteroarilo cíclico fusionado, y cada hidrógeno en R1 es opcionalmente sustituido por uno o más grupos R3.

20. El compuesto de la reivindicación 12, en donde R1 es un grupo –SO2NR4R5.

21. Un compuesto de la formula 3



3

en donde:

R1 es seleccionado de arilo C6- 12, heterarilo de 5- 12 miembros, cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, - O(CR6R7)nR4, - C(O)R4, - C(O)OR4, - CN, - NO2, - S(O)mR4, - SO2NR4R5, - C(O)NR4R5, - NR4(C(O)R5, - C(=NR6)NR4R5, alquilo C1- 8, alquenilo C2- 8, y alquinilo C2- 8; y cada hidrógeno en R1 es opcionalmente substituido por uno o más grupos R3;

R2 es hidrogeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5, y cada hidrógeno en R2 es opcionalmente sustituido por uno o más grupos R8;

R3 es halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5, cada hidrógeno en R3 es opcionalmente sustituido por uno o más grupos R8, y grupos los R3 sobre átomos adyacentes se pueden combinar para formar un arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o grupo heteroalicíclico de 3- 12 miembros;

Cada uno de R4, R5, R6 y R7 es independientemente hidrógeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de nitrógeno pueden junto con el nitrógeno al cual están unidos ser combinados para formar un heteroalicíclico de 13 a 12 miembros o grupo heteroarilo de 5- 12 miembros opcionalmente conteniendo de 1 a 3 heteroátomos adicionales seleccionados de N. O y S; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de carbono puede ser combinados para formar un cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, o grupo

heteroarilo de 5- 12 miembros; y cada hidrógeno en R4, R5, R6 y R7 es opcionalmente sustituido por uno o más grupos R8;

cada R8 es independientemente halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5 - 12 miembros, - CN, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O- (CH2)n(heteroalicíclico de 3- 12 miembros) o - O- (CH2)n(heteroarilo de 5- 12 miembros); y cada hidrógeno en R8 es opcionalmente sustituido por uno o más grupos R11;

A1 es - (CR9R10)n- A2 excepto que:

(i) cuando Y es N y R1 es arilo sustituido o no sustituido o heteroarilo sustituido o no sustituido, A1 es - (CR9R10)n- A2 y n no es cero; y

(ii) cuando Y es N y R2 es H y A1 es m- clorobencilo, R1 es piperazina no sustituida;

cada R9 y R10 es independientemente hidrógeno, halógeno, alquilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5; R9 y R10 se pueden combinar para formar un cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, arilo C6- 12 o anillo de heteroarilo de 5- 12 miembros; y cada hidrógeno en R9 y R10 es opcionalmente sustituido por uno o más grupos R3;

A2 es arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o heteroalicíclico de 3 - 12 miembros, y A2 es opcionalmente sustituido por uno o más grupos R3;

cada R11 es independientemente halógeno, alquilo C1- 12, alcoxilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5- 12 miembros, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O_(CH2)n(heteroalicíclico de 3- 12 miembros), - O- (CH2)n(heteroarilo de 5- 12 miembros) o - CN, y cada hidrógeno en R11 es un generalmente sustituido por uno o más grupos seleccionados de halógeno - OH, - CN, alquilo C1- 12, el cual puede ser parcial o totalmente halogenado, alquilo - O- C1- 12 el cual puede ser total o parcialmente halogenado, - CO, - SO y - SO2;

R1 y R2 se pueden combinar juntos para formar arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12, o grupo heteroalicíclico de 3- 12 miembros;

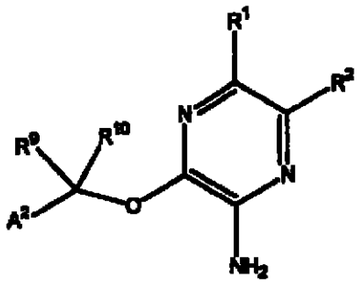
m es 0, 1 o 2;

n es 0, 1, 2, 3 o 4; y

p es 1 o 2;

o una sal, solvato o hidrato farmaceuticamente aceptable del mismo.

22. El compuesto de la reivindicación 21, en donde el compuesto tiene la formula 3a



3a

23. El compuesto de la reivindicación 22, en donde R1 es seleccionado de arilo C6- 12 y heteroarilo de 5- 12 miembros, y cada hidrógeno en R1 es opcionalmente sustituido por uno o más grupos R3.

24. El compuesto de la reivindicación 22, en donde R1 es seleccionado de cicloalquilo C3- 12, heteroaliciclico de 3- 12 miembros, - O(CR6R7)nR4, - C(O)R4, - C(O)OR4, - CN, - NO2, - S(O=mR4, - SO2NR4R5, - C(O)NR4R5, - NR4C(O)R5, - C(=NR6)NR4R5, alquilo C1- 8, alquenilo C2- 8, y alquinilo C2- 8; y cada hidrógeno en R1 es opcionalmente sustituido por uno o más grupos R3.

25. El compuesto de la reivindicación 22, en donde A2 es sustituido por al menos un átomo de halógeno.

26. El compuesto de la reivindicación 22, en donde R2 es hidrógeno, R9 y R10 son independientemente alquilo C14, y A2 es fenilo sustituido por al menos un átomo de halógeno.

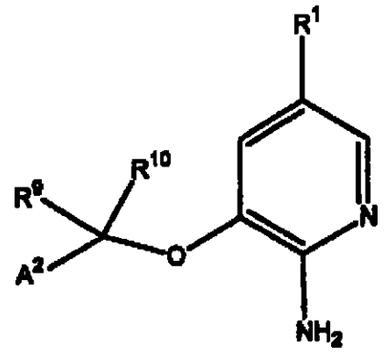
27. El compuesto de la reivindicación 21, en donde R1 es un furano, tiopeno, pirrola, pirrolina, pirrolidina, dioxolano, oxazol, tiazol, imidazolina, imidazolidina, pirazol, pirazolina, pirazolidina, isoxazol, isotiazol, oxadiazol, triazol, tiadiazol, pirano, piridina,

piperidina, dioxano, morfolina, ditiano, tiomorfolina, piridazina, pirimidina, pirazina, piperazina, triazina, tritiano, o grupo fenilo, y cada hidrogeno en R1 es opcionalmente sustituido por uno o más grupos R3.

28. El compuesto de la reivindación 21, en donde R1 es un grupo heteroarilo cíclico fusionado, y cada hidrógeno en R1 es opcionalmente sustituido por uno o más grupos R3.

29. El compuesto de la reivindicación 21, en donde R1 es un grupo –SO2NR4R5.

30. Un compuesto de la formula 4



4

en donde:

R1 es seleccionado de arilo C6- 12, heterarilo de 5- 12 miembros, cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, - O(CR6R7)nR4, - C(O)R4, - C(O)OR4, - CN, - NO2, - S(O)mR4, - SO2NR4R5, - C(O)NR4R5, - NR4(C(O)R5, - C(=NR6)NR4R5, alquilo C1- 8, alquenilo C2- 8, y alquinilo C2- 8; y cada hidrógeno en R1 es opcionalmente substituido por uno o más grupos R3;

R3 es halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5, cada hidrógeno en R3 es opcionalmente sustituido por uno o más grupos R8, y grupos los R3 sobre átomos adyacentes se pueden combinar para formar un arilo

C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o grupo heteroalicíclico de 3- 12 miembros;

Cada uno de R4, R5, R6 y R7 es independientemente hidrógeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de nitrógeno pueden junto con el nitrógeno al cual están unidos ser combinados para formar un heteroalicíclico de 13 a 12 miembros o grupo heteroarilo de 5- 12 miembros opcionalmente conteniendo de 1 a 3 heteroátomos adicionales seleccionados de N. O y S; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de carbono puede ser combinados para formar un cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, o grupo heteroarilo de 5- 12 miembros; y cada hidrógeno en R4, R5, R6 y R7 es opcionalmente sustituido por uno o más grupos R8;

cada R8 es independientemente halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5 - 12 miembros, - CN, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O- (CH2)n(heteroalicíclico de 3- 12 miembros) o - O- (CH2)n(heteroarilo de 5- 12 miembros); y cada hidrógeno en R8 es opcionalmente sustituido por uno o más grupos R11;

cada R9 y R10 es independientemente hidrógeno, halógeno, alquilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5; R9 y R10 se pueden combinar para formar un cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, arilo C6- 12 o anillo de heteroarilo de 5- 12 miembros; y cada hidrógeno en R9 y R10 es opcionalmente sustituido por uno o más grupos R3;

A2 es arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o heteroalicíclico de 3 - 12 miembros, y A2 es opcionalmente sustituido por uno o más grupos R3;

cada R11 es independientemente halógeno, alquilo C1- 12, alcoxilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5- 12 miembros, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O_(CH2)n(heteroalicíclico de 3- 12 miembros), - O-

(CH2)n(heteroarilo de 5- 12 miembros) o - CN, y cada hidrógeno en R11 es un generalmente sustituido por uno o más grupos seleccionados de halógeno - OH, - CN, alquilo C1- 12, el cual puede ser parcial o totalmente halogenado, alquilo - O- C1- 12 el cual puede ser total o parcialmente halogenado, - CO, - SO y - SO2;

m es 0, 1 o 2;

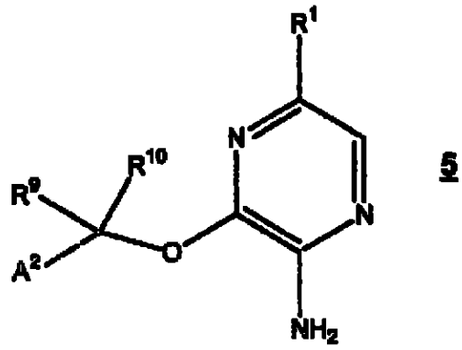
n es 0, 1, 2, 3 o 4; y

p es 1 o 2;

o una sal, solvato o hidrato farmaceuticamente aceptable del mismo.

31. El compuesto de la reivindicación 30, en donde A2 es arilo C6- 12 o heteroarilo de 5- 12 miembros opcionalmente sustituido por uno o más grupos R3.

32. Un compuesto de la formula 5



5

en donde:

R1 es seleccionado de arilo C6- 12, heterarilo de 5- 12 miembros, cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, - O(CR6R7)nR4, - C(O)R4, - C(O)OR4, - CN, - NO2, - S(O)mR4, - SO2NR4R5, - C(O)NR4R5, - NR4(C(O)R5, - C(=NR6)NR4R5, alquilo C1- 8, alquenilo C2- 8, y alquinilo C2- 8; y cada hidrógeno en R1 es opcionalmente substituido por uno o más grupos R3;

R3 es halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - O(CR6R7)nR4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - C(=NR6)NR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5, cada hidrógeno en R3 es opcionalmente sustituido por uno o más grupos R8, y grupos los R3 sobre átomos adyacentes se pueden combinar para formar un arilo

C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o grupo heteroalicíclico de 3- 12 miembros;

Cada uno de R4, R5, R6 y R7 es independientemente hidrógeno, halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de nitrógeno pueden junto con el nitrógeno al cual están unidos ser combinados para formar un heteroalicíclico de 13 a 12 miembros o grupo heteroarilo de 5- 12 miembros opcionalmente conteniendo de 1 a 3 heteroátomos adicionales seleccionados de N. O y S; o cualquiera dos entre R4, R5, R6 y R7 unidos al mismo átomo de carbono puede ser combinados para formar un cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, o grupo heteroarilo de 5- 12 miembros; y cada hidrógeno en R4, R5, R6 y R7 es opcionalmente sustituido por uno o más grupos R8;

cada R8 es independientemente halógeno, alquilo C1- 12, alquenilo C2- 12, alquinilo C2- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5 - 12 miembros, - CN, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O- (CH2)n(heteroalicíclico de 3- 12 miembros) o - O- (CH2)n(heteroarilo de 5- 12 miembros); y cada hidrógeno en R8 es opcionalmente sustituido por uno o más grupos R11;

cada R9 y R10 es independientemente hidrógeno, halógeno, alquilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3- 12 miembros, heteroarilo de 5- 12 miembros, - S(O)mR4, - SO2NR4R5, - S(O)2OR4, - NO2, - NR4R5, - (CR6R7)nOR4, - CN, - C(O)R4, - OC(O)R4, - NR4C(O)R5, - (CR6R7)nC(O)OR4, - (CR6R7)nNCR4R5, - NR4C(O)NR5R6, - NR4S(O)pR5 o - C(O)NR4R5; R9 y R10 se pueden combinar para formar un cicloalquilo C3- 12, heteroalicíclico de 3- 12 miembros, arilo C6- 12 o anillo de heteroarilo de 5- 12 miembros; y cada hidrógeno en R9 y R10 es opcionalmente sustituido por uno o más grupos R3;

A2 es arilo C6- 12, heteroarilo de 5- 12 miembros, cicloalquilo C3- 12 o heteroalicíclico de 3 - 12 miembros, y A2 es opcionalmente sustituido por uno o más grupos R3;

cada R11 es independientemente halógeno, alquilo C1- 12, alcoxilo C1- 12, cicloalquilo C3- 12, arilo C6- 12, heteroalicíclico de 3 - 12 miembros, heteroarilo de 5- 12 miembros, alquilo - O- C1- 12, cicloalquilo - O- (CH2)nC3- 12, arilo - O- (CH2)nC6- 12, - O_(CH2)n(heteroalicíclico de 3- 12 miembros), - O-

(CH2)n(heteroarilo de 5- 12 miembros) o - CN, y cada hidrógeno en R11 es un generalmente sustituido por uno o más grupos seleccionados de halógeno - OH, - CN, alquilo C1- 12, el cual puede ser parcial o totalmente halogenado, alquilo - O- C1- 12 el cual puede ser total o parcialmente halogenado, - CO, - SO y - SO2;

m es 0, 1 o 2;

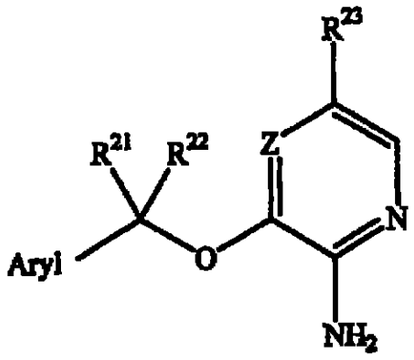
n es 0, 1, 2, 3 o 4; y

p es 1 o 2;

o una sal, solvato o hidrato farmaceuticamente aceptable del mismo.

33. El compuesto de la reivindicación 32, en donde A2 es arilo C6- 12, o heteroarilo de 5- 12 miembros opcionalmente sustituido por uno o más grupos R3.

34. Un compuesto de la formula 6



(6)

en donde,

Z es CH o N;

arilo es un arilo opcionalmente fusionado o un grupo heteroarilo opcionalmente fusionado el cual es opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consta de un halógeno,- OR24, - COR24, - COOR24, - CONR24R25, - CN, - NO2, - S(O)mR24, - SO2NR24R25, perfluoroalquilo, alquilo inferior, cicloalquilo, heterociclo, alquenilo, alquinilo, arilo, - NR24R25, - NR24C(O)R25 y - NRS(O)p25;

R21 y R22 son independientemente seleccionados del grupo que consta de hidrógeno, halógeno, COR24, - COOR24, - CONR24R25, - CN, perfluoroalquilo, alquilo inferior, cicloalquilo, heterociclo, alquenilo, alquinilo, y arilo;

R23 es seleccionado del grupo que consta de:

un arilo opcionalmente fusionado, heteroarilo, grupo alicíclico o heterocíclico, opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consta de un halógeno, - (CH2)n- OR24, - COR24, - COOR24, - CONR24R25, - CN, - NO2, - S(O)mR24, - SO2NR24R25, perfluoroalquilo, - O- perfluoroalquilo, alquilo inferior, cicloalquilo, heterociclo, heeteroarilo, alquenilo, alquinilo, arilo,- (CH2)n- NR24R25, - NR24C(O)R25 y - NR24S(O)p25, en donde dichos sustituyentes de heterociclo, heteroarilo y arilo puede ser opcionalmente sustituidos por un grupo seleccionado del grupo que consta de alquilo inferior, halógeno, C(O)NR24R25, NR24R25, NR24C(O)R25 y NR24S()pR25;

- OR24, - COR24, - COOR24, - CN, - NO2, - S(O)mR24, - SO2NR24R25, perfluoroalquilo, cicloalquilo, heterociclo, alquenilo, y alquinilo;

R24 y R25 so independientemente seleccionados del grupo que consta de hidrógeno, alquilo inferior, cicloalquilo, alquenilo, alquinilo, arilo, aminoalquilo, alquilaminoalquilo, alquilaminocicloalquilo, dialquilaminoalquilo, y - (CH2)n- heterociclo, en donde dicho - (CH2)n- heterociclo puede adicionalmente se sustituido con uno o más de alquilo inferior, - (CH2)n- hidroxilo, heterociclo y - C(O)R26,

o R24 y R25 se pueden combinar para formar un anillo heterociclico de 5 a 6 miembros con uno o más heteroátomos seleccionados del grupo que consta de N, O, S(O) y SO2, dicho anillo heterocíclico de 5 a 6 miembros puede ser opcionalmente sustituido con alquilo inferior, - (CH2)n- heterociclo, cicloalquilo, halo, - (CH2)n- NR26R27, amino, - C(O)R26, - NR26- C(O)OR27 y - NR26 - C(O)R27;

en donde R26 y R27 son independientemente seleccionados del grupo que consta de hidrógeno, alquilo inferior, - (CH2)n- cicloalquilo y - C(O)- (CH2)n- OH;

excepto que cuando Z es N y R21 y R22 son H y arilo es m- clorofenilo, R23 no es piperazina;

m es 0, 1 o 2;

n es 0, 1, 2 o 3;

p es 1 o 2;

o una sal farmaceuticamente aceptable del mismo.

35. El compuesto de la reivindicación 34, en donde R23 es arilo o heteroarilo.

36. Un compuesto seleccionado del grupo que consta de:

4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenol; 3- (2,6- dicloro- benciloxi)- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- [3- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (1H- indol- 4- il)- piridin- 2- ilamina; 3- [2- cloro- 6- (1H- indol- 4- il)- benciloxi]- 5- (1H- indol- 4- il)- piridin- 2- ilamina; éster tert- butilico del ácido 2- [amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- pirrola- 1- carboxilico; 3- (2,6- dicloro- benciloxi)- 5- (1H- pirrol- 2- il)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (4- fluoro- fenil)- piridin- 2- ilamina;
3- (2,6- dicloro- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (3- fluoro- fenil)- piridin- 2- ilamina; 5- (4- amino- fenil)- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina; N- {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- metanosulfonamida; N- {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- acetamida; 3- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenol; 3- (2,6- dicloro- benciloxi)- 5- (4- metoxi- fenil)- piridin- 2- ilamina; 5- (3- amino- fenil)- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (3- trifluorometoxi- fenil)- piridin- 2- ilamina; 2- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenol; 3- (2,6- dicloro- benciloxi)- 5- (2- fenoxi- fenil)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (3,4- difluoro- fenil)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (2- isopropil- fenil)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (2- trifluorometil- fenil)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (2- metoxi- fenil)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (4- trifluorometil- fenil)- piridin- 2- ilamina; N- {2- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- metanosulfonamida; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- metanol; 3- (2,6- dicloro- benciloxi)- 5- (2- trifluorometoxi- fenil)- piridin- 2- ilamida; 3- (2,6- dicloro- benciloxi)- 5- (4- metil- tiofen- 2- il)- piridin- 2- ilamida; 5- (2- benciloxi- fenil)- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamida; 3- (2,6- dicloro- benciloxi)- 5- (3- metoxi- fenil)- piridin- 2- ilamida; 3- (2,6- dicloro- benciloxi)- 5- (1H- indol- 2- il)- piridin- 2- ilamida; 5- (4- benciloxi- 3- fluoro- fenil)- 3- (2,6- dicloro- benciloxi)- piridin- 2- ilamida; ácido 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- benzoico; 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- N- (2- dietilamino- etil)- benzamida; 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- N- (3- dietilamino- propil)- benzamida; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil-

pirrolidin- 1- il)- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [4- (2- hidroxi- etil)- piperidin- 1- il)- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(3R)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- ciclopropilaminometil- piperidin- 1- il]- metanona; 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- N- (2- hidroxi- 3- pirrolidin- 1- il- propil)- benzamida; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2(3- fluoro- piperidin- 1- il- ilmetil)- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- (4- ciclopropil- piperazin- 1- il)- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- [(ciclopropilmetil- amino)- metil]- pirrolidin- 1- il}- metanona; 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- N- [ciclopropilmetil- N- (2R)- pirrolidin- 2- ilmetil- benzamida; 4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- N- (2- hidroxi- 3- pirrolidin- 1- il- propil)- N- metil- benzamida; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- {(3R)- 3- hidroxi- pirrolidin- 1- ilmetil]- pirrolidin- 1- il}- metanona; ácido 3- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- benzoico; {3- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il}- metanona; ácido 2{4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenoxi}- acetico; 2- {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenoxi}- 1- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- etanona; 2- {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenoxi}- 1- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- etanona; 3- (2,6- dicloro- benciloxi)- 5- (1H- indol- 5- il)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- [3- (1- metil- 1,2,3,6- tetrahidro- piridin- 4- il)- 1H- indol- 5- il]- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- [3- (1- metil- piperidin- 4- il)- 1H- indol- 5- il]- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (3- morfolin- 4- ilmetil- 1H- indol- 5- il)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (3- piperidin- 1- ilmetil- 1H- indol- 5- il)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (3- pirrolidin- 1- ilmetil- 1H- indol- 5- il)- piridin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- (3- dietilaminometil- 1H- indol- 5- il)- piridin- 2- ilamina; éster tert- butilico del ácido (1- {5- [6- amino- 5- (2,6- dicloro- benciloxi)-

piridin- 3- il]- 1H- indol- 3- ilmetil}- (3R)- pirrolidin- 3- il)- carbamico; 3- (2,6- dicloro- benciloxi)- 5- [(2,6- - dimetil- morfolin- 4- ilmetil)- 1H- indol- 5- il]- piridin- 2- ilamina; N- (1- {5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 3- ilmetil}- (3R)- pirrolidin- 3- il)- acetamida; 1- (4{5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 3- ilmetil}- piperazin- 1- il)- etanona; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (1H- indol- 5- il)- piridin- 2- ilamina; 1- (4- {5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- 1H- indol- 3- ilmetil}- piperazin- 1- il)- etanona; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- [3- (2- dimetil- morfolin- 4- ilmetil)- 1H- indol- 5- il]- piridin- 2- ilamina; N- (1- {5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- 1H- indol- 3- ilmetil}- (3S)- pirrolidin- 3- il)- acetamida; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (3- piperidin- 1- ilmetil- 1H- indol- 5- il)- piridin- 2- ilamina; 3- (2- cloro3,6- difluoro- benciloxi)- 5- (3- morfolin- 4- ilmetil- 1H- indol- 5- il]- piridin- 2- ilamina; 3- (2- cloro3,6- difluoro- benciloxi)- 5- (3- pirrolidin- 1- ilmetil- 1H- indol- 5- il)- piridin- 2- ilamina; éster etilico del ácido 5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carboxilico; ácido 5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carboxilico; {5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- il}- (4- metil- piperazin- 1- il)- metanona; {5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- il}[(3R)- 3- metilamino- pirrolidin- 1- il]- metanona; {5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- il}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; (2- pirrolidin- 1- il- etil)- amida del ácido 5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carboxilico; (2- morfolin- 4- il- etil)- amida del ácido 5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carboxilico; éster tert- butilo del ácido (1- {5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carbonil}- (3S)- pirrolidin- 3- il)- carbamico; (2- hidroxi- 3- pirrolidin- 1- il- propil)- amida del ácido 5- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- 1H- indol- 2- carboxilico; 4(6- amino- 5- benciloxi- piridin- 3- il)- fenol; 3- benciloxi- 5- fenil- piridin- 2- ilamina; 3- (3- metoxi- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2- cloro- 4- fluoro- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2- cloro- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2,5- dicloro- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2- cloro- 5- trifluorometil- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2,4- dicloro- 5- fluoro- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2- cloro- 3- trifluorometil- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (3,4- dicloro- 5- fluoro- benciloxi)- 5- fenil- piridin- 2- ilamina;

2- (2- amino- 5- fenil- piridin- 3- iloximetil)- benzonitrilo; 3- (2- cloro- 6- fluoro- 3- metil- benciloxi)- 5- fenil- piridin- 2- ilamina; 5- fenil- 3- (2,3,6- trifluoro- benciloxi)- piridin- 2- ilamina; 3- (2,6- difluoro- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2,6- difluoro- 3- metil- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (3- cloro- 2,6- difluoro- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (2- cloro- 6- fluoro- benciloxi)- 5- fenil- piridin- 2- ilamina; 3- (3- fluoro- 4- metoxi- benciloxi)- 5- fenil- piridin- 2- ilamina; N- [3- (2- amino- 5- fenil- piridin- 3- iloximetil)- fenil]- metanosulfonamida; 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- 3- (3- nitro- benciloxi)- piridin- 2- ilamina; 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- 3- (3- naftaleno- 1- ilmetoxi)- piridin- 2- ilamina; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina; 2- {2- amino- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 3- iloxi}- N- (4- isopropil- fenil)- 2- fenil- acetamida; 3- (5- cloro- benzo[b]tiofen- 3- ilmetoxi)- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina; 4- [6- amino- 5- (4- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}[(2R)- 2- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- fluoro- 6- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (5- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; (4- {6- amino- 5- [1- (2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- bromo- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; 4- [6- amino- 5- (2- 6- difluoro- benciloxi)- piridin- 3- il]- fenol.; 3- (2,6- difluoro- benciloxi)- 5- (1H- indol- 4- il)- piridin- 2- ilamina; 3- (2,6- difluoro- benciloxi)- 5- [4- (2- morfolin- 4- il- etoxi-)- fenil]- piridin- 2- ilamina, ácido 4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- benzoico, {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; ester etilico del ácido {4- [6- amino- 5- (2,6- fluoro- benciloxi)- piridin- 3- il]- fenoxi- acetico; ácido {4- [6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenoxi- acetico; 2- {4- [6- amino- 5- (2,6- fluoro- benciloxi)- piridin- 3- il]- fenoxi}- 1- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- etanona; 2- {4- [6- amino- 5- (2,6- difluoro-

benciloxi)- piridin- 3- il]- fenoxi}- 1- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- etanona; 4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenol; 4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- fenol; 4- [6- amino- 5- (2- 4- dicloro- benciloxi)- piridin- 3- il]- fenol; 2- [2- amino- 5- (4- hidroxi- frnil)- piridin- 3- iloximetil]- benzonitrilo; 4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenol; 4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenol; 4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenol; 4- [6- amino- 5- (4- tert- butilo- benciloxi)- piridin- 3- il]- fenol; N- {4- [6- amino- 5- (2- ciano- benciloxi)- piridin- 3- il]- fenil}metanosulfonamida; 2- [2- amino- 5- (4- metanosulfonilamino- fenil)- piridin- 3- iloximetil]- benzamida; ácido 2- [2- amino- 5- (4- metanosulfonilamino- fenil)- piridin- 3- iloximetil]- benzoico; N- (4- {6- amino- 5- [2- (4- metilpiperazina- 1- carbonil)- benciloxi]- piridin- 3- il}- fenil)- metanosulfonamida; 2- [2- amino- 5- (4- metanosulfonilamino- fenil)- piridin- 3- iloximetil]- N- (2- hidroxi- etil)- benzamida; 2- [2- amino- 5- (4- metanosulfonilamino- fenil)- piridin- 3- iloximetil]- N- isobutil- benzamida; acido 4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- benzoico; {4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; 1- (4- {4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- benzoil}- piperazin- 1- il)etanona; 4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida; 4- [6- amino- 5- (2- cloro- 6- fluoro- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- propil)- benzamida; ácido 4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- benzoico; {4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenil}[(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; {4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- fenil}- (4- metil-

piperazin- 1- il)- metanona; 1- (4- {4[6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- benzoil}- piperazin- 1- il)- etanona; 4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida; 4- [6- amino- 5- (2- cloro- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- il- propil)- benzamida; ácido 4- [6- amino- 5- (2- ciano- benciloxi)- piridin- 3- il]- benzoico, 2- {2- amino- 5- [4- ((2R)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carbonil)- fenil]- piridin- 3- iloximetil}- benzonitrilo; 2- {2- amino- 5- [4- ((2S)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carbonil)- fenil]- piridin- 3- iloximetil}- benzonitrilo; 2- {2- amino- 5- [4- ((3S)- 3- dimetilamino- pirrolidina- 1- carbonil)- fenil]- piridin- 3- iloximetil}- benzonitrilo; 2- {2- amino- 5- [4- ((3S)- 3- amina- pirrolidina- 1- carbonil)- fenil]- piridin- 3- iloximetil}- benzonitrilo; 2- {2- amino- 5- [4- (4- metil- piperazina- 1- carbonil)- fenil]- piridin- 3- iloximetil}- benzonitrilo; 2- {5- [4- (4- acetil- piperazina- 1- carbonil)- fenil]- 2- amino- piridin- 3- iloximetil}- benzinitrilo; 4- [6- amino- 5- (2- ciano- benciloxi)- piridin- 3- il]- N- (1- metil- piperidin- 4- il)- benzamida; 4- [6- amino- 5- (2- ciano- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- il- propil)- benzamida; ácido 4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- benzoico; {4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- fenil}[(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; 1- (4- {4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- benzoil}- piperazin- 1- il)- etanona; 4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- N- (1- metil- 1- piperidin- 4- il)- benzamida; 4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- N- (1- morfolin- 4- il- 1- etil)- benzamida; 4- [6- amino- 5- (2,4- dicloro- benciloxi)- piridin- 3- il]- N- (1- morfolin- 4- il- 1- propil)- benzamida; acido {4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]metanona; {4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]metanona; [(3S)- 3- amino- pirrolidin- 1- il]- {4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- metanona; {4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il]metanona; {4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il]metanona; 1- (4{4- [6-

amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- benzoil}- piperazin- 1- il]etanona; 4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- N- (1- metil- piperidin- 4- il]- benzamida; {4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil]- benzamida; {4- [6- amino- 5- (2- trifluorometil- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- il- propil]- benzamida; ácido 4- [6- amino- 5- (4- #tert- butilo- benciloxi)- piridin- 3- il]- benzoico; {4- [6- amino- 5- (4- tert- butilo- benciloxi)- piridin- 3- il]fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (4- tert- butilo- benciloxi)- piridin- 3- il]fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (4- tert- butilo- benciloxi)- piridin- 3- il]fenil}- [(3R)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (4- tert- butilo- benciloxi)- piridin- 3- il]fenil}- (4- metil- piperazin- 1- il)- metanona; 1- (4{4- [6- amino- 5- (4- tert- butilo- benciloxi)- piridin- 3- il]- benzoil}- piperazin- 1- il)- etanona; 4- [6- amino- 5- (4- tert- butilo- benciloxi)- piridin- 3- il]- N- (1- metil- piperidin- 4- il)- benzamida; 4- [6- amino- 5- (4- tert- butilo- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida; 4- [6- amino- 5- (4- tert- butilo- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- il- propil)- benzamida; ácido 4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- benzoico; 4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il]- metanona; {4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il]- metanona; 1- (4- {4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- benzoil}- piperazin- 1- il)- etanona; 4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- etil)- benzamida; 4- [6- amino- 5- (2- cloro- 4- fluoro- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- propil)- benzamida; ácido 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzoico; {4- [6- amino- 5- (2- cloro- 3,4- difluoro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (4- amino- piperidin- 1- il)- metanona; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il)-

metanona; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il])- metanona; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il])- metanona; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(3R)- 3- amino- 1- pirrolidin- 1- il])- metanona; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il])- metanona; 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (1- metil- piperidin- 4- il])- benzamida; 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (2- pirrolidin- 1- il- etil)- benzamida; 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (3- pirrolidin- 1- propil)- benzamida; 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida; 4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- propil-)- benzamida; ácido 3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzoico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il)- metanona; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (4- amino- piperidin- 1- il)- metanona; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(3R)- 3- amino- pirrolidin- 1- il]- metanona; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- [(3S)- amino- pirrolidin- 1- il]- metanona; 3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (1- metil- piperidin- 4- il)- benzamida; 3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (2- pirrolidin- 1- il- etil)- benzamida; 3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (3- pirrolidin- 1- il- propil)- benzamida; 3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida; 3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- N- (3- morfolin- 4- propil)- benzamida; N- [2- (4- acetil- piperazin- 1- il)- etil]- 3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- benzamida; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- [4- (1,1- dioxo- 1λ^6- isotiazolidin- 2- il)- fenil]- piridin- 2-

ilamina; 3- (2,6- dicloro- benciloxi)- 5- [4- (1,1- dioxo- 1λ^6- isotiazolidin- 2- il)- fenil]- piridin- 2- ilamina; 5- [4- (1,1- dioxo- 1λ^6- isotiazolidin- 2- il)- fenil]- 3- (2- fluoro- 6- trifluorometil- benciloxi)- piridin- 2- ilamina; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- dietilamino- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- ciclopropilamino- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- pirrolidin- 1- il- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- morfolin- 4- il- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- piperidin- 1- il- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- dietilamino- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- (4- acetil- piperazin- 1- il)- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- (ciclopropilmetil- amino)- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- [(3R)- 3- hidroxi- pirrolidin- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- [(2S)- 2- hidroximetil- pirrolidin- 1- il]- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- 4- (2- hidroxi- acetil)- piperazin- 1- il]- etanosulfónico; {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- (4- acetil- piperazin- 1- il)- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- pirrolidin- 1- il- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- morfolin- 4- il- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- dietilamino- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- dimetilamino- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- piperidin- 1- iletanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- [(3R)- 3- hidroximetil- pirrolidin- 1- il]- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6-

difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- [4- hidroxi- acetil)- piperazin- 1]- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- [(3R)- 3- hidroxi- pirrolidin- 1- il]- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- (ciclopropilmetil- amino)- etanosulfónico; {3- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- amida del ácido 2- ciclopropilano- etanosulfónico; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (2- dimetilaminometil- fenil)- piridin- 2- ilamina; compuesto con ácido trifluoro- acetico; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (3- pirrolidin- 1- il- fenil)- piridin- 2- ilamina; compuesto con ácido trifluoro- acetico; N- {4- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- metanosulfonamida; compuesto con ácido trifluoro- acetico; ácido {5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofeno- 2- carboxilico; {5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofen- 2- il}- (4- metil- piperazin- 1-)- metanona; {5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofen- 2- il}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; (1- metil- piperidin- 4- il)- amida del ácido 5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofeno- 2- carboxilico; {5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofen- 2- il}- (3,5- metil- piperazin- 1- il)- metanona; (2- pirrolidin- 1- il- etil)- amida del ácido 5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofeno- 2- carboxilico; {5- [6- amino- 5- (2- cloro- 3,6- difluoro- benciloxi)- piridin- 3- il]- tiofen- 2- il}- (4- pirrolidin- 1- il-)- metanona; ácido 4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- benzoico; {4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin –1- piperidin- 1- il)- metanona; 4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- N- (1- metil- piperidin- 4- il)- benzamida; {4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona; {4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (3- dimetilamino- pirrolidin- 1- il)- metanona; {4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; 4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- N- (2- morfolin- 4- il- etil)- benzamida; {4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; N- [2- (4- acetil- piperazin- 1- il)- etil]- 4- [6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]- benzamida; (4- {6- amino- 5- [1- (2-

cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- piperidin- 1- il- etanosulfónico; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- dimetilamino- etanosulfónico; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- ciclopropilamino- etanosulfónico; ácido 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- benzoico; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- [(2R)- 2- pirrolidin- 1- il)- metanona; 4- {6- amino- 5[1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (1- metil- piperidin- 4- il)- benzamida; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- [(3R)- 3- amino- pirrolidin- 1- il]- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (3,5- dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- cloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- ciclopropilamino- etanosulfónico; (4- {6- amino- 5- [1- (2,6- cloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- dimetilamino- etanosulfónico; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- [(3R)- 3- hidroxi- pirrolidin- 1- il)]- etanosulfónico; y sales, hidratos y solvatos farmacéuticamente aceptables de los mismos.

37. Un compuesto seleccionado del grupo que consta de de 4- [5- amino- 6- (2,6- dicloro- benciloxi)- pirazin- 2- il]- fenol; 3- (2,6- dicloro- benciloxi)- 5- [4- (1,1- dioxo- 1λ^6- isotiazolin- 2- il)- fenil]- pirazin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- [3- (2- morfolin- 4- il- etoxi)- fenil]- pirazin- 2- ilamina; 5- (4- amino- fenil)- 3- (2,6- dicloro- benciloxi)- pirazin- 2- ilamina; 3- (2,6- dicloro- benciloxi)- 5- [3- (2- morfolin- 4- il- etoxi)- fenil]- pirazin- 2- ilamina; ácido 5- [4- amino- 6- (2,6- dicloro- benciloxi)- pirazin- 2- il]- benzoico; {4- [5- amino- 6- (2,6- dicloro- benciloxi)- pirazin- 2- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; 4- [5- amino- 6- (2,6- dicloro- benciloxi)- pirazin- 2- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- morfolin- 4- il- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6-

difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- piperidin- 1- il- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- pirrolidin- 1- il- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- [(3R)- 3- hidroxi- pirrolidin- 1- il]- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- [(2S)- 2- hidroximetil- pirrolidin- 1- il]- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- (ciclopropilmetil- amino)- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- dimetilamino- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- dietilamino- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- (4- acetil- piperazin- 1- il)- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- [4- (2- hidroxi- acetil)- piperazin- 1- il]- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- ciclopropilamino- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- [(3R)- 3- hidroximetil- pirrolidin- 1- il]- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- (4- acetil- piperazin- 1- il)- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- piperidin- 1- il- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- dietilamino- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- morfolin- 4- il- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- pirrolidin- 1- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- dimetilsmino- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- [4- (2- hidroxi- acetil)- piperazin- 1- il]- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- (ciclopropilmetil- amino)- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]-

fenil}- amida del ácido 2- [(3R)- 3- hidroxi- pirrolidin- 1- il]- etanosulfónico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- amida del ácido 2- ciclopropilamino- etanosulfónico; ácido 4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- benzoico; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; 4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (2- pirrolidin- 1- il- etil)- benzamida; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il]- metanona; N- [2- (4- acetil- piperazin- 1- il)- etil]- 4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- benzamida; 4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (3- pirrolidin- 1- il- propil)- benzamida; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3R)- 3- dimetilamino- pirrolidin- 1- il]- metanona; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (3- morfolin- 4- il- propil)- benzamida; 4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (1- metil- piperidin- 4- il)- benzamida; 4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (2- morfolin- 4- il- etil)- benzamida; {4- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; ácido 3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- benzoico; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3R)- 3- amino- pirrolidin- 1- il]- metanona; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3S)- 3- amino- pirrolidin- 1- il]- metanona; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3,5- dimetil- piperazin- 1- il)- metanona; 3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (3- morfolin- 4- il- propil)- benzamida; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(3S)- 3- dimetilamino- pirrolidin- 1- il]- metanona; 3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (2- pirrolidin- 1- il- etil)- benzamida; 3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)-

pirazin- 2- il]- N- (1- metil- piperidin- 4- il)- benzamida; {3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- fenil}- [(2S)- pirrolidin- 1- ilmetil- pirrolidin- 1- il]- metanona; 3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (2- morfolin- 4- etil)- benzamida; N- [2- (4- acetil- piperazin- 1- il)- etil]- 3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- benzamida; 3- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- N- (3- pirrolidin- 1- il- propil)- benzamida; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (1H- indol- 5- il)- pirazin- 2- ilamina; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (3- pirrolidin- 1- ilmetil- 1H- indol- 5- il)- pirazin- 2- ilamina; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (3- dietilaminometil- 1H- indol- 5- il)- pirazin- 2- ilamina; 1- (4- {5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- 1H- indol- 3- ilmetil}- piperazin- 1- il)- etanona; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- [3- (2,6- dietil- morfolin- 4- ilmetil)- 1H- indol- 5- il]- pirazin- 2- ilamina; N- (1- {5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- 1H- indol- 3- ilmetil}(3S)- pirrolidin- 3- il)- acetamida; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (3- piperidin- 1- ilmetil- 1H- indol- 5- il)- pirazin- 2- ilamina; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- (3- morfolin- 4- ilmetil- 1H- indol- 5- il)- pirazin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi)- fenil]- pirazin- 2- ilamina; compuesto con ácido trifluoro- acetico; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- pirazin- 2- ilamina; compuesto con ácido trifluoro- acetico; N- (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- metanosulfonamida; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il]- fenil}- amida del ácido 2- pirrolidin- 1- il- etanosulfónico; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido 2- piperidin- 1- il- etanosulfónico; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido 2- (ciclopropilmetil- amino)- etanosulfónico; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido 2- [(3R)- 3- hidroxi- pirrolidin- 1- il]- etanosulfónico; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido 2- dimetilamino- etanosulfónico; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido 2- morfolin- 4- il- etanosulfónico; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido 2- dietilamino- etanosulfónico; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2-

il}- fenil)- amida del ácido 2- ciclopropilamino- etanosulfónico; ácido 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- benzoico; (3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}fenil)- [(3S)- 3- amino- pirrolidin- 1- il)- m- etanona; (3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}fenil)- [(3r)- 3- amino- pirrolidin- 1- il)- m- etanona; (3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]pirazin- 2- il}fenil)- [(2R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; N- [2- (4- acetil- piperazin- 1- il)- etil]- 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- benzamida; (3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}fenil)- [(2S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; ácido 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- benzoico; 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4- il)- benzamida; 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; (3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; ácido 4[5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- benzoico; 4- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- N- (1- metil- piperidin- 4- il)- benzamida; y sales, hidratos y solvatos farmacéuticamente aceptables de los mismos.

38. Un compuesto seleccionado del grupo que consta de (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; N- [2- (4- acetil- piperazin- 1- il)- etil]- 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- benzamida; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((s)- 3- amino- pirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- amino- piperidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 3- hidroxi- pirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 3- hidroxi- pirrolidin- 1- il)- metanona; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 2- hidroximetil- pirrolidin- 1- il)- metanona; 4-

{6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- dietilamino- etil)- benzamida; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; ácido 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- benzoico; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}fenil)- (4- metil- piperazin- 1- il)- metanona; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (1- metil- piperidin- 4- il)- benzamida; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; N- [2- (4- acetil- piperazin- 1- il)- etil]- 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 3- il}- benzamida; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 3- amino- pirrolidin- 1- il)- metanona; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (3- morfolin- 4- il- propil)- benzamida; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- piperidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- dietilamino- etanosulfónico; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- (ciclopropilmetil- amino)- etanosulfónico; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- ((R)- 3- hidroxi- pirrolidin- 1- il)- etanosulfónico; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- ciclopropilamino- etanosulfónico; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 2- dietilamino- etanosulfónico;

Ácido 4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- benzoico; 4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida; 4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (1- metil- piperidin- 4- il)- benzamida; (4- {6- amino- 5- [1-

(2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; 4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; (4- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; (4- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 3- amino- pirrolidin- 1- il)- metanona; ácido 3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- benzoico; (3- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; (3- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona; 3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (1- metil- piperidin- 4- il)- benzamida; (3- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; 3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; 3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; (3- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 3- amino- pirrolidin- 1- il)- metanona; 3- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida; (3- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (3- {6- amino- 5- [1- (2,- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- [3- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [4- (2- morfolin- 1- il- etoxi)- fenil]- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- {4- [2- (1- metil- pirrolidin- 2- il)- etoxi]- fenil}- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3-

fluoro- fenil)- etoxi]- 5- [4- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [3- (2- morfolin- 4- il- etoxi)- fenil]- piridin- 2- ilamina; 1- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenoxi)- 3- morfolin- 4- il- propan- 2- ol; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [4- (1- metil- piperidin- 3- ilmetoxi)- fenil]- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [4- (1- metil- piperidin- 4- iloxi)- fenil]- piridin- 2- ilamina; N- (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- metanosulfonamida; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- [1,1- dioxo- 1 lamba*6*- isotiazolidin- 2- il)- fenil]- piridin- 2- ilamina; N- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- metanosulfonamida; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- fenil]- piridin- 2- ilamina; N- (4- {6- amino- 5- [(R)- 1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- metanosulfonamida; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- tiofen- 3- il- piridin- 2- ilamina; 5- benzo[b]tiofen- 2- il- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 4- metil- piperazina- 1- carboxilico; 1- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (2- pirrolidin- 1- il- etil)- urea; 1- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (2- hidroxi- etil)- urea; 1- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (2- morfolin- 4- il- etil)- urea; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido (R)- 3- amino- pirrolidina- 1- carboxilico; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido (S)- 3- amino- pirrolidina- 1- carboxilico; 1- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (1- metil- piperidin- 4- il)- urea; 1- (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (1- metil- piperidin- 4- il)- urea; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido (R)- 3- amino- pirrolidina- 1- carboxilico; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido (S)- 3- amino- pirrolidina- 1- carboxilico; 1- (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (2- hidroxi- etil)- urea; (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido 4- metil- piperazina- 1- carboxilico; 1- (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (2- pirrolidin- 1- il- etil)- urea; 1- (4- {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- (2-

morfolin- 4- il- etil)- urea; (4- {6- amino- 5- [1- (2- cloro- 3,6- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- amida del ácido (R)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxilico; ácido 3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- benzoico; (3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; (3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; 3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida; (3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; 3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; N- [2- (4- acetil- piperazin- 1- il)- etil]- 3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida; 3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (1- metil- piperidin- 4- il)- benzamida; (3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; (3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 3- amino- pirrolidin- 1- il)- metanona; (3- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona; ácido 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- benzoico; 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida; (4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 2- pirrolidin- 1- il)- metanona; ácido 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- benzoico; 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin- 4- il- etil)- benzamida; (4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (1- metil- piperidin- 4- il)- benzamida; (4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; N- [2- (4- acetil- piperazin- 1- il)- etil]- 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- benzamida; 4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- N- (3-

pirrolidin- 1- il- propil)- benzamida; (4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((S)- 3- aminopirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- (R)- 3- amino- pirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- amida del ácido (S)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxilico; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- amida del ácido 4- metil- piperazin- 1- carboxilico; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- amida del ácido 4- pirrolidin- 1- il- piperidina- 1- carboxilico; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- amida del ácido (3R, 5S)- 3,5- dimetil- piperazina- 1- carboxilico; 1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 3- (1- metil- piperidin- 4- il)- urea; 1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 3- (3- pirrolidin- 1- il- propil)- urea; 1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 3- (2- pirrolidin- 1- il- etil)- urea; 1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 3- (2- morfolin- piperidin- 4- il- etil)- urea; 1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 3- (3- morfolin- 4- il- propil)- urea; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- amida del ácido (R)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxilico;3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3- dimetilamino- prop- 1- inil)- piridin- 2- ilamina; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- urea; N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- piperidin- 1- il- acetamida; N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- morfolin- 4- il- acetamida; N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- pirrolidin- 1- il- acetamida; N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- ((R)- 3- hidroxi- pirrolidin- 1- il)- acetamida; N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- (4- hidroxi- piperidin- 1- il)- acetamida; N- (3- {6- amino- 5- [1- (2,6- dicloro- 3-

fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- dimetilamino- acetamida; N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- 2- dietilamino- acetamida; 2- (4- acetil- piperazin- 1- il)- N- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- prop- 2- inil)- acetamida; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- amida del ácido 4- metil- piperazin- 1- carboxilico; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- amida del ácido (3R, 5S)- 3,5- dimetil- piperazin- 1- carboxilico; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- amida del ácido (3R, 5S)- 3,5- dimetil- piperazin- 1- carboxilico; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- amida del ácido (R)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxilico; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- amida del ácido (S)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxilico; 1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- 3- (2- morfolin- 4- il- propil)- urea; 1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- 3- (2- pirrolidin- 1- il- etil)- urea; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1,1- dimetil- prop- 2- inil)- amida del ácido 4- pirrolidin- 1- il- piperidina- carboxilico; ciclohexilamida del ácido 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- propinoico; isopropilamida del ácido 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- propinoico; 4- (3- amino- 3- metil- but- 1- inil)- 2- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- fenilamida; (4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- il)- metanona; (4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; 4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- N- (1- metil- piperidin- 4- il)- benzamida; 4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- N- (2- pirrolidin- 1- etil)- benzamida; 4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- N- (2- morfolin-

4- il- etil)- benzamida; 4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; 4- {6- amino- 5- [1- (3- fluoro- 2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- N- (3- morfolin- 4- il- propil)- benzamida; 6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- nicotinonitrile; 6- amino- 5- [1- (2,6- dicloro- 3- ciano- fenil)- etoxi]- nicotinonitrile; 5- aminometil- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- ilmetil}- amida del ácido (R)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxilico; N- {6- amino- 5- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- ilmetil}- metanosulfonamida; N- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- ilmetil}- acetamida; N- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- ilmetil}- 4- metil- bencenosulfonamida; 5- aminometil- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- vinil- piridin- 2- ilamina; (S)- 1- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}etano- 1,2- diol; (R)- 1- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}etano- 1,2- diol; ++3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (1H- pirazol- 4- il)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [1- (2- pirrolidin- 1- il- etil)- 1H- pirazol- 4- il]- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [1- (2- diisopropilamino- etil)- 1H- pirazol- 4- il]- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [1- (2- morfolin- 4- il- etil)- 1H- pirazol- 4- il]- piridin- 2- ilamina; 5- bromo- 3- (3- fluoro- 2- metoxi- benciloxi)- piridin- 2- ilamina; 5- bromo- 3- [1- (3- fluoro- 2- metoxi- fenil)- etoxi]- piridin- 2- ilamina; {4- [6- amino- 5- (3- fluoro- 2- metoxi- benciloxi)- piridin- 3- il]- fenil}- ((3R,5S)- 3,5- dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (3- fluoro- 2- metoxi- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R,5S)- 3,5- dimetil- piperazin- 1- il)- metanona; 5- bromo- 3- (3- fluoro- 2- isopropoxi- benciloxi)- piridin- 2- ilamina; {4- [6- amino- 5- (3- fluoro- 2- isopropoxi- benciloxi)- piridin- 3- il]- fenil}- ((3R,5S)- 3,5- dimetil- piperazin- 1- il)- metanona; 5- (4- amino- fenil)- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina; ester metilo del ácido (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenoxi)- acetico; 2- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenoxi)- 1- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- etanona; 2- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenoxi)- 1- ((R)- 3- hidroxi- pirrolidin- 1- il)- etanona; ester tert- butilo del ácido 4- [2- (4- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenoxi)- acetil]- piperazina- 1- carboxilico; 2- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)-

etoxi]- piridin- 3- il}- fenoxi)- 1- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- etanona; 5- bromo- 3- (3- fluoro- 6,7,8,9- tetrahidro- 5H- benzocicloheptен- 5- iloxi)- piridin- 2- ilamina; {4- [6- amino- 5- (3- fluoro- 6,7,8,9- tetrahidro- 5H- benzocicloheptен- 5- iloxi)- piridin- 3- il]- fenil}- ((3R,5S)- 3,5- dimetil- piperazin- 1- il)- metanona; 3- (3- fluoro- 6,7,8,9- tetrahidro- 5H- benzocicloheptен- 5- iloxi)- 5- [4- (2- pirrolidin- 1- il- etoxi)- fenil]- piridin- 2- ilamina; N- {4- [6- amino- 5- (3- fluoro- 6,7,8,9- tetrahidro- 5H- benzocicloheptен- 5- iloxi)- piridin- 3- il]- fenil}metanosulfonamida; 3- (3- fluoro- 6,7,8,9- tetrahidro- 5H- benzocicloheptен- 5- iloxi)- 5- (1H- pirazol- 4- il)- piridin- 2- ilamina; 5- bromo- 3- [1- (2- cloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina; 3- [1- (2- cloro- 3- fluoro- fenil)- etoxi]- 5- [4- (2- pirrolidin- 1- il- etoxi-)- fenil]- piridin- 2- ilamina; 5`- benciloxi- [2,3]bipiridinil- 6`- ilamina; 5- benciloxi- [3,3`]bipiridinil- 6- ilamina; 3- benciloxi- 5- pirimidin- 5- il- piridin- 2- ilamina; 5`- benciloxi- [2,3]bipiridinil- 6`- ilamina; 5- benciloxi- [3,3`]bipiridinil- 6,6´- ilamina;diamina; 5- (2- cloro- benciloxi)- [2,3`]bipiridinil- 6´- ilamina; 5- (2- cloro- benciloxi)- [3,3`]bipiridinil- 6- ilamina; 3- (2- cloro- benciloxi)- 5- oirimidin- 5- il- piridin- 2- ilamia; 5- (2- cloro- benciloxi)- [3,3`]bipiridinil- 6,6´- diamina; 5´- (4- cloro- benciloxi)- [2,3`]bipiridinil- 6´- ilamina; 5- (4- cloro- benciloxi)- [3,3`]bipiridinil- 6- ilamina; 3- (4- cloro- benciloxi)- 5- pirimidin- 5- il- piridin- 2- ilamina; 5- (4- cloro- benciloxi)- [3,3`]bipiridinil- 6,6´- diamina; 5´- (2- cloro- 3,6- difluoro- benciloxi)- [2,3`]bipiridinil- 6´- ilamina; 5´- (2- cloro- 3,6- difluoro- benciloxi)- [3,3`]bipiridinil- 6- ilamina; 5- (2- cloro- 3,6- difluoro- benciloxi)- [2,4`]bipiridinil- 6´- ilamina; 3- (2- cloro- 3,6- difluoro- benciloxi)- 5- pirimidin- 5- il- piridin- 2- ilamia; 5- (2- cloro- 3,6- difluoro- benciloxi)- [3,3`]bipiridinil- 6,6´- diamina; 5´- (2,6- dicloro- benciloxi)- [2,3`]bipiridinil- 6´- ilamina; 5´- (2,6- dicloro- benciloxi)- [3,3`]bipiridinil- 6- ilamina; 5- (2,6- dicloro- benciloxi)- [3,4`]bipiridinil- 6´- ilamina; 3- (2,6- dicloro- benciloxi)- 5- pirimidin- 5- il- piridin- 2- ilamina; 5- (2,6- dicloro- benciloxi)- [3,3`]bipiridinil- 6,6´- diamina; 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [3,3`]bipiridinil- 6,6´- diamina; {6´- amino- 5´- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [2,3´]bipiridin- 4- il}- (4- metil- piperazin- 1- il)- metanona; {6´- amino- 5´- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [2,3´]bipiridin- 6- il}- (4- metil- piperazin- 1- il)- metanona; {6´- amino- 5´- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [3,3´]bipiridin- 5- il}- (4- metil- piperazin- 1- il)- metanona; {6´- amino- 5´- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [3,3´]bipiridin- 6- il}- (4- metil- piperazin- 1- il)- metanona; {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [3,4´]bipiridin- 2´- il}- (4- metil- piperazin- 1-

il)- metanona; 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [3,3']bipiridinil- 6,6'- diamina; {6'- amino- 5'- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [2,3']bipiridin- 5- il}- (4- metil- piperazin- 1- il)- metanona; {6'- amino- 5'- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [2,3']bipiridin- 4- il}- (4- metil- piperazin- 1- il)- metanona; {6'- amino- 5'- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [2,3']bipiridin- 6- il}- (4- metil- piperazin- 1- il)- metanona; {6'- amino- 5'- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [3,3']bipiridin- 5- il}- (4- metil- piperazin- 1- il)- metanona; {6- amino- 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [3,4']bipiridin- 2'- il}- (4- metil- piperazin- 1- il)- metanona; 5'- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [2,3']bipiridin- 6'- ilamina; 5'- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [2,3']bipiridin- 6'- ilamina; 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [3,3']bipiridin- 6- ilamina; 5'- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- pirimidin- 5- il- piridin- 2- ilamina; {6'- amino- 5'- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [2,3']bipiridin- 5- il}- (4- metil- piperazin- 1- il)- metanona; 5- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [3,4']bipiridin- 6- ilamina; 5- benciloxi- 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- [3,3']bipiridin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- (2- etil- butoxi)- piridin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- (3- metil- butoxi)- piridin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- butoxi- piridin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- propoxi- piridin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- ciclohexilmetoxi- piridin- 2- ilamina; 6- amino- 5- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- piridin- 3- ol; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- (2- ciclohexil- etoxi)- piridin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- isobutoxi- piridin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- fenetiloxi- piridin- 2- ilamina; 3- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- 5- (piridin- 4- ilmetoxi)- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 2- fluoro- benzonitrilo; 4- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- piperidin- 4- ol; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- piperidin- 1- il- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- pirrolidin- 1- il- metanona; ester metilo del ácido (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- 3- metil- benzoico; 3- [1- (2,6-

dicloro- 3- fluoro- fenil)- etoxi]- 5- [4- (dimetil- piperazin- 1- ilmetil)- fenil]- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 3,5- dimetoxi- fenil)- (dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 2- fluoro- fenil)- (dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 3- fluoro- fenil)- (dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 3- metil- fenil)- (dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- metil- [1,4]diazepan- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- [1,4]diazepan- 1- il- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- piperazin- 1- il- metanona; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- vinil- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R)- 3,4- dihidroxi- pirrolidin- 1- il)- metanona; 5- [(1- bencil- pirrolidin- 3- ilamino)- metil]- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N- azetidin- 3- il- benzamida; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- N,N- dimetil- bencenosulfonamida; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (6- metoxi- 1H- benzoimidazol- 2- il)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (6- metoxi- 1- metil- 1H- benzoimidazol- 2- il)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [4- (4- metil- [1,4]diazepano- 1- sulfonil)- fenil]- piridin- 2- ilamina; amida del ácido 6{6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 1- metil- 1H- indazol- 3- carboxilico; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (1- metil- 1H- pirazol- 4- il)- piridin- 2- ilamina; 5- (3- cloro- fenil)- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (4- fluoro- 3- metil- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3- trifluorometil- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3- trifluorometoxi- fenil)- piridin- 2- ilamina; 5- benzo[1,3]dioxol- 5- il- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina; 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenol; 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- metanol; 3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- benzonitrilo; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3- metoxi- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3,5- dicloro- fenil)- piridin-

2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,5- dimetil- fenil)- piridin- 2- ilamina; 5- (5- cloro- 2- metoxi- fenil)- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,5- dimetil- fenil)- piridin- 2- ilamina; 5- (3- cloro- 4- fluoro- fenil)- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,5- dimetil- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (5- fluoro- 2- metoxi- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3- isopropil- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3,4- dicloro- fenil)- piridin- 2- ilamina; 4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- benzonitrilo; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3,4- difluoro- fenil)- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- ((2R,6S)- 2,6- dimetilmorfolin- 4- il)- metanona; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2- etoxi- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (5,2- dimetoxi- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,4- dimetoxi- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2- trifluorometil- fenil)- piridin- 2- ilamina; 5- (2- cloro- fenil)- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,5- dimetil- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2- trifluorometoxi- fenil)- piridin- 2- ilamina; 1- (2- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- etanona; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2- fluoro- fenil)- piridin- 2- ilamina; (2- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- metanol; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- o- tolil- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2- metoxi- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,6- dimetil- fenil)- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- morfolin- 4- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 2- cloro- fenil- ((3R,5S)- dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- 2- metil- fenil)- ((3R,5S)- dimetil- piperazin- 1- il)- metanona; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- [4- ((2R, 6S)- 2,6- dimetil- morfolin- 4- ilmetil)- fenil]- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (4- morfolin- 4- ilmetil- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3,5- dimetil- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- m- tolil- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3,4- dimetoxi- fenil)- piridin- 2- ilamina; 5- bifenil- il- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina; 5- (3,5-

bis- trifluorometil- fenil)- 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- 5- (3,4- dicloro- fenil)- piridin- 2- ilamina; 1- (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- etona; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3,5- difluoro- fenil)- piridin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (2,5- dicloro- fenil)- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2,6- dicloro- 4- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (3- etoxi- fenil)- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- (3,5- dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (3- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- (3,5- dimetil- piperazin- 1- il)- metanona; 7- [4- (3,5- dimetil- piperazin- 1- carbonil)- fenil]- 2- femil- 4H- pirido[3,2- b]pxazin- 3- ona; (4- {6- amino- 5- (3- fluoro- 2- trifluorometil- benciloxi)- piridin- 3- il]etoxi]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona; {4- {6- amino- 5- (2,6- difluoro- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona; [4- {6- amino- 5- benciloxi- piridin- 3- il)- fenil]- (3,5- dimetil- piperazin- 1- il)- metanona; (4- {6- amino- 5- [1- (2- clor- 3,6- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- etil- piperazin- 1- il)- metanona; [4- {6- amino- 5- benciloxi- piridin- 3- il)- fenil]- (4- etil- piperazin- 1- il)- metanona; {4- [6- amino- 5- (2- metil- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona; ester metilico del ácido 3- {2- amino- 5- [4- (4- pirrolidin- 1- piperidina- 1- carbonil)- fenil]- piridin- 3- iloximetil}benzoico; ester metilico del ácido 3- {2- amino- 5- [4- (3,5- dimetil- piperazina- 1- carbonil)- fenil]- piridin- 3- iloximetil}benzoico; {4- [6- amino- 5- (2- metil- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; [4- (6- amino- 5- ciclohexilmetoxi- piridin- 3- il)- fenil]- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 4- (1- {2- amino- 5- [4- (4- pirrolidin- 1- il- piperidina- 1- il- carbonil)- fenil]- piridin- 3- iloxi}- etil)- [2- (3- hidroxi- fenil)- etil]- benzamida; 4- (1- {2- amino- 5- [4- (4- pirrolidin- 1- il- piperidina- 1- il- carbonil)- fenil]- piridin- 3- iloxi}- etil)- [2- (2,6dicloro- fenil)- etil]- benzamida; 4- (1- {2- amino- 5- [4- (4- pirrolidin- 1- il- piperidina- 1- il- carbonil)- fenil]- piridin- 3- iloxi}- etil)- (1- bencil- piperidin- 4- il)- benzamida; 4- (1- {2- amino- 5- [4- (4- pirrolidin- 1- il- piperidina- 1- il- carbonil)- fenil]- piridin- 3- iloxi}- etil)- [3- (2- oxo- pirrolidin- 1- il)- propil]- benzamida; (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- etil- piperazin- 1- il)- metanona; {4- [6- amino- 5- (2,6- dicloro- benciloxi)- piridin- 3- il]- fenil}- (3,5- dimetil- piperazin- 1- il)- metanona; (6- amino- 3- aza-

biciclo[3.1.0]hex- 3- il)- (4- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- metanona; 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 6'- (2- morfolin- 4- il- etoxi)- [3,3']bipiridinil- 6- ilamina; 6'- amino- 5'- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 1- (2- pirrolidin- 1- il- etil)- 1H- [3,3']bipiridinil- 6- ona; 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 6'- (2- pirrolidin- 1- il- etoxi)- [3,3']bipiridinil- 6- ilamina; 6'- amino- 5'- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 1- [2- (1- metil- pirrolidin- 2- il)- etil]- 1H- [3,3']bipiridinil- 6- ona; (4- {6- amino- 5- [1- (2,4,6- trimetil- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2- cloro- 6- fluoro- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (4- fluoro- fenil)- piridin- 2- ilamina; 6'- amino- 5'- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 1H- [3,3']bipiridinil- 6- ona; 5`- bromo- 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- [3,3']bipiridin- 6- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (4- dimetilamino- fenil)- piridin- 2- ilamina; 5- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 2'- metoxi- [3,3']bipiridin- 6- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (1H- indol- 5- il)- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2,6- dicloro- fenil)- propoxi]- piridin- 3- il}- fenil)- (3,5- dimetil- piperazin- 1- il)- metanona; [4- {6- amino- 5- benciloxi- piridin- 3- il)- fenil]- (4- pirrolidin- 1- il- piperiidn- 1- il)- metanona; 3- [1- (2,6- dicloro- 3- fluoro- benciloxi)- 5- tiazol- 2- piridin- 2- ilamina; (4- {6- amino- 5- [1- (2- fluoro- 6- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 3- (2,6- dicloro- 3- fluoro- benciloxi)- 5- (1- metil- 1H- imidazol- 2- il)- piridin- 2- ilamina; {4- [6- amino- 5- (2,4,6- trimetil- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; {4- [6- amino- 5- (2,3,5,6- tetrametil- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; {4- [6- amino- 5- (2,4,6- trifluoro- benciloxi)- piridin- 3- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; (4- {6- amino- 5- [1- (2- fluoro- 6- trifluorometil- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 6- amino- 5- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- N- metil- nicotidina; 6- amino- 5- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- N- (2- morfolin- 4- il- etil)- nicotidina; (4- {6- amino- 5- [1- (2,4,5- trifluoro- fenil)- propoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; (4- {6- amino- 5- [1- (6- cloro- 2- fluoro- 3- metil- fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; ácido 3- (1- {2- amino- 5- [4- (4- pirrolidin- 1- il- piperidin-

1- carbonil)- fenil]- piridin- 3- iloxi}- etil)- benzoico; y sales, hidratos y solvatos farmaceuticamente aceptables de los mismos.

39. Un compuesto seleccionado del grupo que consta de

3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; 3- {5- amino- 6- [1- (2- cloro- 3,6- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; 3- {5- amino- 6- [1- (2- cloro- 3,6- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4- il)- benzamida; 3- {5- amino- 6- [1- (2,- cloro- 3- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; 3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 1- il- etil)- benzamida; 3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- benzamida; N- [2- (4- acetil- piperazin- 1- il)- etil- 3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- benzamida; (3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; (3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; (3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; (3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- ((S)- 2- pirrolidin- 1- il)- metanona; (3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona; (3- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- ((S)- 3- amino- pirrolidin- 1- il)- metanona; ácido 4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- benzoico; 4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il))- metanona; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il))- metanona; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- ((R)- 3- amino- pirrolidin-

1- il)- metanona; 4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4- il)- benzamida; 4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; 4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- benzamida; [2- (4- acetil- piperazin- 1- il)- etil]- 4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- benzamida; ácido 2- [4- (2- hidroxi- acetil)- piperazin- 1-]- etanosulfónico; 4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida; ácido 3- [5- amino- 6- [1- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- benzoico; {3- {5- amino- 6- [1- (3- fluoro- 2- trifluorometil- benciloxi)- pirirazin- 2- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 3- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- N- {2- [etil- (2- metoxi- etil)- amino]- etil}- benzamida; {3- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirirazin- 2- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; 3- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- N- (3- pirrolidin- 1- il- propil)- benzamida; N- [2- (4- acetil- piperazin- 1- il)- 3- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirazin- 2- il]- benzamida; {4- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirirazin- 2- il]- fenil}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; {3- {5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirirazin- 2- il]- fenil}- (4- metil- piperazin- 1- il)- metanona; {3- [5- amino- 6- (3- fluoro- 2- trifluorometil- benciloxi)- pirirazin- 2- il]- fenil}- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (3- [5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; (3- [5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- (3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4- il)- benzamida; 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- benzamida; 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- morfolin- 4- il- propil)- benzamida; (3- [5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- (4- ciclopropilamino- piperidin- il)- metanona; 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- ((S)- 2- hidroxi- 3- morfolin- 4- il- propil)- benzamida; 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- ((R)- 2- hidroxi- 3- pirrolidin- 1- il- propil)- benzamida; (3- {6- amino- 5- [1- (2,6- dicloro- 3- fluoro-

fenil)- etoxi]- piridin- 3- il}- fenil)- (4- pirrolidin- 1- piperidin- 1- il)- metanona; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- amida del ácido 2- dietilamino- etanosulfónico; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- amida del ácido 2- (4- hidroxi- piperidin- 1- il)- etanosulfónico; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- amida del ácido 2- dimetilamino- etanosulfónico; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- amida del ácido 2- ((R- 3- hidroxi- pirrolidin- 1- il)- etanosulfónico; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- amida del ácido 2- pirrolidin- 1- iletanosulfónico; ácido (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirirazin- 2- il}- benzoico; 4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- ((R)- 2- hidroxi- 3- pirrolidin- 1- il- propil)- benzamida; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- ciclopropilamino- 1- piperidin- 1- il)- metanona; 3- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- ((S)- 2- hidroxi- 3- pirrolidin- 1- il- propil)- benzamida; 4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- ((R)- 2- hidroxi- 3- morfolin- 4- il- propil)- benzamida; 4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4)- benzamida; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((S)- 2- pirrolidin- 1- metil- pirrolidin- 1- il)- metanona; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- benzamida; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- metil- 1- piperazin- 1- il)- metanona; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((3R,5S)- 3,5- dimetil- piperazin- 1- il)- metanona; ácido 4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- benzoico; (4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; 4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- benzamida; (4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; 4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4- il)- benzamida; (4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((3R, 5S)- 3,5- dimetil-

piperazin- 1- il)- metanona; (4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((S)- 2- pirrolidin- 1- il)- metanona; (4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; (4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (R)- 3- aminopirrolidin- 1- il)- metanona; cloruro de hidrogeno (4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((S)- 3- aminopirrolidin- 1- il)- metanona; 4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; 4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; ácido 3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- benzoico; 3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (1- metil- piperidin- 4- il)- benzamida; 3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (2- pirrolidin- 1- il- etil)- benzamida; (3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; 3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- benzamida; (3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((S)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- pirrolidin- 1- ilpiperidin- 1- il)- metanona; N- [2- (4- acetil- piperazin- 1- il)- etil]- 4- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- benzamida; N- [2- (4- acetil- piperazin- 1- il)- etil]- 3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- benzamida; (3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; 3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- N- (3- pirrolidin- 1- il- propil)- benzamida; (3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((S)- 3- amino- pirrolidin- 1- il)- metanona; sal de hidrocloruro (3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- ((R)- 3- amino- pirrolidin- 1- il)- metanona; (3- {5- amino- 6- [1- (2,6- dicloro- fenil)- etoxi]- pirazin- 2- il}- fenil)- (4- metil- piperazin- 1- il)- metanona; 1- (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- 3- (2- morfolin- 4- il- etil)- urea; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- amida del ácido (R)- 2- pirrolidin- 1- ilmetil- pirrolidina- 1- carboxilico; 1- (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- 3- (2- pirrolidin- 1- il- etil)- urea; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- amida del ácido 4- metil- piperazin- 1- carboxilico; 1- (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2-

il}- fenil)- 3- (2- hidroxi- etil)- urea; (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirirazin- 2- il}- fenil)- amida del ácido (S)- 3- amino- pirrolidina- 1- carboxilico; 1- (4- {5- amino- 6- [1- (2- cloro- 3,6- difluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- 3- (1- metil- piperidin- 4- il)- urea; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido 4- metil- piperazin- 1- carboxilico; 1- (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}fenil)- 3- (2- hidroxi- etil)- urea; (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- fenil)- amida del ácido (S)- 3- amino- pirrolidin- 1- carboxilico; 1- (4- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}fenil)- 3- (1- metil- piperidin- 4- il)- urea; ácido {5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofeno- 2- carboxilico ; {5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofen- 2- il}- (4- metil- piperazin- 1- il)- metanona {5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofen- 2- il}- (4- pirrolidin- 1- il- piperidin- 1- il)- metanona; {5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofen- 2- il}- ((3R, 5S)- 3,5- dimetil- piperazin- 1- il)- metanona; {5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofen- 2- il}- ((R)- 2- pirrolidin- 1- ilmetil- pirrolidin- 1- il)- metanona; (2- morfolin- 4- il- etil)- amida del ácido 5- [5- amino- 6- (2- cloro- 3,6- difluoro- benciloxi)- pirazin- 2- il]- tiofeno- 2- carboxilico; trifluoroacetato 3- [(2,6- dicloro- 3- fluorofenil)- etoxi]- 5- {5- [(4- metilpiperazin- 1- il)- carbonil]piridin- 2- il}pirazin- 2- amina, 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- piridin- 4- il- pirazin- 2- ilamina; 3- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- 5- (1H- pirrol- 2)- ilamina; (6- [5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il]- tiofen- 2- il}- piridin- 3- il)- (4- metil- piperazin- 1- il)- metanona; (2- [5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- piridin- 4- il)- (4- metil- piperazin- 1- il)- metanona; (6- [5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- piridin- 2- il)- (4- metil- piperazin- 1- il)- metanona; (5- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- piridin- 3- il)- (4- metil- piperazin- 1- il)- metanona; (4- [5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- piridin- 2- il)- (4- metil- piperazin- 1- il)- metanona; 6- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- nicotinamida; 5- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (2- morfolin- 4- il- etil)- nicotinamida; 6- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- N- (3- morfolin- 4- il- propil)- nicotinamida; 5- {5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}-

N- (3- morfolin- 4- il- propil)- nicotinamida; (6- [5- amino- 6- [1- (2,6- dicloro- 3- fluoro- fenil)- etoxi]- pirazin- 2- il}- piridin- 3- il)- (4- isopropil- piperazin- 1- il)- metanona; y sales, hiratos y solvatos farmaceuticamente aceptables de los mismos.

40. Un compuesto seleccionado del grupo que consta de los compuestos mostrados en la tabla 5 y sales, hidratos y solvatos farmaceuticamente aceptables de los mismos.

41. Un compuesto seleccionado del grupo que consta de los compuestos mostrados en la Tabla 6 y sales, hidratos y solvatos farmaceuticamente aceptables de los mismos.

42. Un compuesto seleccionado del grupo que consta de los compuestos mostrados en la Tabla 7 y sales, hidratos y solvatos farmeceuticamente aceptables de los mismos.

43. Un compuesto seleccionado del grupo que consta de los compuestos mostrados en la Tabla 8 y y sales, hidratos y solvatos farmeceuticamente aceptables de los mismos.

44. Un método para tratar crecimiento celular anormal en un mamífero, el método comprendiendo la administración a un mamífero de una cantidad terapéuticamente efectiva de un compuesto, sal, hidrato o solvato de cualquiera de las reivindicaciones 1-43.

45. El método de la reivindicación 44, en donde el crecimiento celular anormal es cáncer.

46. El método de la reivindicación 45, en donde el cáncer es seleccionado del cáncer pulmonar, cáncer óseo, cáncer pancreático, cáncer de piel, cáncer de cabeza y cuello, melanoma cutáneo o intraocular, cáncer uterino, cáncer ovárico, cáncer rectal, cáncer de la región anal, cáncer estomacal, cáncer del colon, cáncer de mama, carcinoma de las trompas de Falopio, carcinoma del endometrio, carcinoma de la cérvix, carcinoma de la vagina, carcinoma de la vulva, enfermedad de Hodgkin, cáncer del esófago, cáncer del intestino delgado, cáncer del sistema endocrino, cáncer de la glándula tiroides, cáncer de glándula paratiroides, cáncer de la glándula adrenal, sarcoma de tejidos blandos, cáncer de la uretra, cáncer del pene, cáncer de la próstata, leucemia crónica o aguda, linfomas linfocíticos, cáncer de la vejiga, cáncer del riñón o uréter, carcinoma de células

renales, carcinoma de la pelvis renal, neoplasmas del sistema nervioso central (SNC), linfoma del sistema nervioso central primario, tumores del eje espinal, glioma del tallo cerebral, adenoma pituitario, y combinaciones de los mismos.

47. El método de la reivindicación 45, En donde el cáncer es seleccionado de tumores estromales gastrointestinales, carcinoma de células renales, cáncer de mama, cáncer colorectal, cáncer pulmonar de células no pequeñas, tumores neuroendócrinos, cáncer tiroideo, cáncer pulmonar de células pequeñas, mastocitosis, glioma, sarcoma, leucemia mieloide aguda, cáncer prostático, linfoma, y combinaciones de los mismos.

48. El método de la reivindicación 44, en donde el método además comprende co-administración de un agente anti- tumoral seleccionado del grupo que consta de inhibidores mitóticos, agentes alquilantes, anti- metabolitos, antibióticos intercaladores, inhibidores de factor de crecimiento, inhibidores del ciclo celular, enzimas, inhibidores de la topoisomerasa, modificadores de respuesta biológica, anticuerpos, citotóxicos, anti- hormonas, anti- andrógenos y mezclas de los mismos.

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
BETH A. BURROUS
FOLEY & LARDNER
WASHINGTON HARBOUR
3000 K STREET, N.W., SUITE 500
WASHINGTON, DC 20007-5101

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY REPORT ON PATAENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	08 NOV 2004
Applicant's or agent's file reference 034536-0989	IMPORTANT NOTIFICATION

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US04/05495	26 February 2004 (26.02.2004)	26 February 2003 (26.02.2003)

Applicant

SUGEN, INC.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary report on patentability and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

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For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the *PCT Applicant's Guide*.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed invention is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230	Authorized officer Zachary C. Tucker Telephone No. (703) 308-0196

Form PCT/IPEA/416 (January 2004)

PATENT COOPERATION TREATY

S81

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
BETH A. BURROUS
FOLEY & LARDNER
WASHINGTON HARBOUR
3000 K STREET, N.W., SUITE 500
WASHINGTON, DC 20007-5101

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY REPORT ON PATAENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Rule 71.1)

Date of mailing (*day/month/year*)	
Applicant's or agent's file reference 034536-0989	IMPORTANT NOTIFICATION

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US04/05495	26 February 2004 (26.02.2004)	26 February 2003 (26.02.2003)

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Form PCT/IPEA/416 (January 2004)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 034536-0989	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/US04/05495	International filing date *(day/month/year)* 26 February 2004 (26.02.2004)	Priority date *(day/month/year)* 26 February 2003 (26.02.2003)
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 31/4965, 31/44; C07D 401/00, 403/00, 405/00, 409/00, 411/00, 413/00, 417/00, 419/00, 211/72 and US Cl.: 514/255.05, 255.06, 339, 349; 544/405, 408; 546/276.7, 277.4, 280.4, 283.4, 297		
Applicant SUGEN, INC.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *(sent to the applicant and to the International Bureau)* a total of ___ sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☒ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))
      1, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
27 September 2004 (27.09.2004)	04 November 2004 (04.11.2004)
Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230	Authorized officer Zachary C. Tucker Telephone No. (703) 308-0196

Form PCT/IPEA/409 (cover sheet)(January 2004)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/05495

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____ , which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:
pages 1-72 and 74-274 as originally filed/furnished
pages* 73 received by this Authority on 27 September 2004 (27.09.2004)
pages* NONE received by this Authority on _____

☒ the claims:
pages 275-311 as originally filed/furnished
pages* NONE as amended (together with any statement) under Article 19
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☐ the drawings:
pages NONE as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*): _____

** If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/05495

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 1-31 and 44-48

because:

☐ the said international application, or the said claim Nos. ____ relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. ____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. ____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 1-31 and 44-48

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No
PCT/US04/05495

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 32-43	YES
	Claims NONE	NO
Inventive Step (IS)	Claims 32-43	YES
	Claims NONE	NO
Industrial Applicability (IA)	Claims 32-43	YES
	Claims NONE	NO

2. Citations and Explanations (Rule 70.7)

WO 03/000666 (CHIANG et al) discloses a compound which is structurally similar to the compounds in claims 32-43 at page 83, in lines 27-28, but this compound excluded from claim 32 by the proviso in that claim, and is not one of the species named in claims 36-39.

Therefore, the subject matter of claims 32-43 satisfies the requirements of PCT Articles 33(2), 33(3) and 33(4).

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
BETH A. BURROUS
FOLEY & LARDNER
WASHINGTON HARBOUR
3000 K STREET, N.W., SUITE 500
WASHINGTON, DC 20007-5101

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(PCT Rule 71.1)

Date of mailing (*day/month/year*)	
Applicant's or agent's file reference 034536-0989	**IMPORTANT NOTIFICATION**

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US04/05495	26 February 2004 (26.02.2004)	26 February 2003 (26.02.2003)

Applicant

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The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed invention is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

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Facsimile No. (703)305-3230	Telephone No. (703) 308-0196

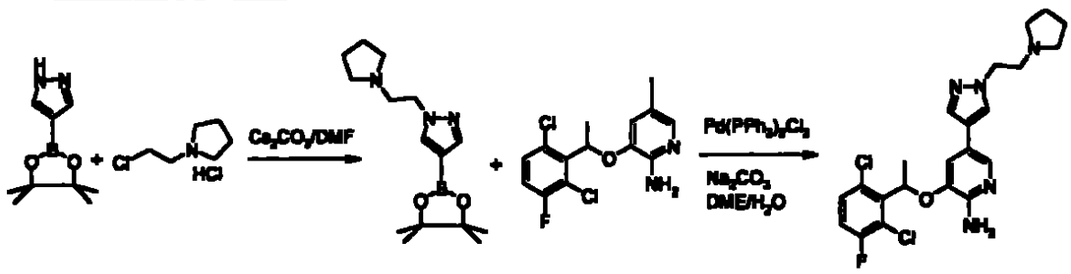
Form PCT/IPEA/416 (January 2004)

IPEA/US 27 SEP 2004

6. To a stirred solution of 4-[6-amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid methyl ester (1.4 g, 3.2 mmol) in warm IPA (72 mL) was added H_2O (38 mL) containing LiOH (0.68 g, 16.2 mmol). The reaction was heated to reflux for 3.5 hr. The reaction was neutralized and diluted with EtOAc (200 mL) and extracted upon cooling. The organic layer was washed with brine (50 mL), dried over Na_2SO_4 and concentrated under vacuum to yield 4-[6-Amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid (1.2 g, 2.8 mmol, 88%). ^{1}H NMR (MeOD, 300 MHz) δ 1.75 (d, 3H, J, 6.2 Hz), 4.88-4.93 (m, 1H), 7.01 (d, 1H, *J*, 1.8 Hz), 7.39 (d, 2H, *J*, 8.3 Hz), 7.52-7.67 (m, 3H), 7.80 (d, 1H, *J*, 1.8 Hz), 7.97 (d, 2H, *J*, 8.3 Hz).

7. Preparation of amide compounds: A stirring solution of 4-[6-Amino-5-[1-(3-fluoro-2-trifluoromethyl-phenyl)-ethoxy]-pyridin-3-yl]-benzoic acid (50 mg, 0.12 mmol), EDC (27.0 mg, 0.13 mmol) and HOBt (18.0 mg, 0.13 mmol) in DMF (2 mL) was added to a two dram vial containing NHR_1R_2 (0.12 mmol). The reaction was stirred at room temperature for 18 hr. The reaction was then diluted with CH_2Cl_2 (3 mL) and partitioned with H_2O. The organic was separated washed with saturated NaCl (1 x 2 mL) and saturated $NaHCO_3$ (1 x 2 mL). The organic was concentrated to dryness under vacuum. The material was purified using column chromatography (silica gel, 99:1 to 95:5 CH_2Cl_2/MeOH). The fractions containing product were concentrated under vacuum to yield amide compounds.

General Procedure 14:



1: To a mixture of 1-(2-chloroethyl)pyrrolidine hydrochloride (200 mg, 1.18 mmol) and 4-[4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)]-1H-pyrazole (229 mg, 1.19 mmol) in DMF (6 mL) was added Cs_2CO_3. The mixture was stirred at room temperature overnight. Water (10 mL) was then added to the mixture. The product was extracted with EtOAc (3 x 10 mL). The combined extracts were then washed with brine (5 x 10 mL) to remove the DMF, then dried over Na_2SO_4, and concentrated (142 mg, 41% yield).

2: To a mixture of 3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-iodo-pyridin-2-ylamine (200 mg, 0.468 mmol), pinacol boronic ester (1.2 eq), Na_2CO_3 (149 mg, 1.41 mmol) in water (1.25 mL), and dimethyl ethyl glycol (3.75 mL, 0.1M) was added $Pd(PPh_3)_2Cl_2$ (16 mg, 0.020 mmol) in a microwave reaction vessel. The system was degassed and charged with nitrogen. The mixture was stirred at 160°C in a microwave apparatus for 15 minutes. The mixture was cooled to room temperature followed by the addition of water (10 mL). The product was extracted with EtOAc (3 x 20 mL), dried over Na_2SO_4, and concentrated. The crude product was purified by reverse phase HPLC with 0.1% TFA in water and acetonitrile.

AMENDED SHEET

588

THE INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY
IN THE UNITED STATES RECEIVING OFFICE
UNDER THE PATENT COOPERATION TREATY

Applicants	:	SUGEN, INC., et al.
International Application No.	:	PCT/US2004/005495
International Filing Date	:	26 February 2004 (26.02.04)
Title of the Invention	:	AMINOHETEROARYL COMPOUNDS AS PROTEIN KINASE INHIBITORS

AMENDMENT UNDER ARTICLE 34

Attn: Mamie Holmes

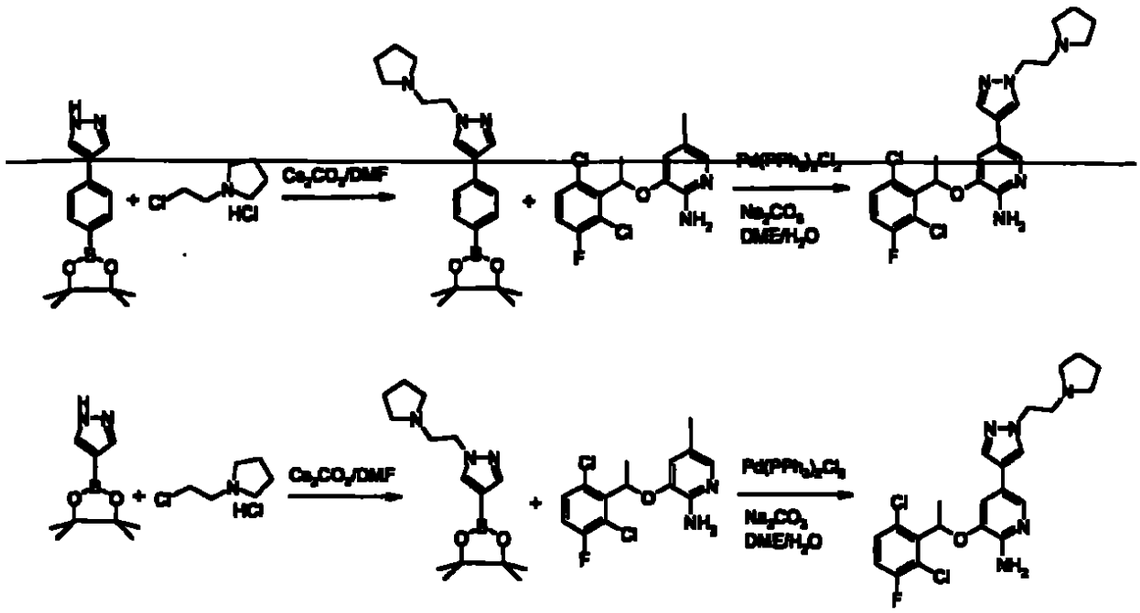
Mail Stop PCT
Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450
Sir/Madam:

The Attorneys for the Applicants respectfully requests the replacement of page 73 of the application with the enclosed replacement sheet page 73.

Amendments to the Specification:

The change to the specification is shown below and replacement sheet page 73 is attached hereto.

Paragraph starting at page 73, line 18-24, with the following rewritten paragraph.



1: To a mixture of 1-(2-chloroethyl)pyrrolidine hydrochloride (200 mg, 1.18 mmol) and 4-[4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-~~phenyl~~]-1H-pyrazole (229 mg, 1.19 mmol) in DMF (6 mL) was added Cs_2CO_3. The mixture was stirred at room temperature overnight. Water (10 mL) was then added to the mixture. The product was extracted with EtOAc (3 x 10 mL). The combined extracts were then washed with brine (5 x 10 mL) to remove the DMF, then dried over Na_2SO_4, and concentrated (142 mg, 41% yield).

REMARKS

Applicant respectfully requests that the foregoing amendments be made prior to examination of the present application.

In the specification, a paragraph has been amended on page 73, lines 18-24. One skilled in the art would recognize that the structures originally presented were a typographical error and that based on the structure of the end product, the starting materials were inadvertently represented in error.

Applicant believes that the present application is now in condition for allowance. Favorable consideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date 27 September 2004

By _____

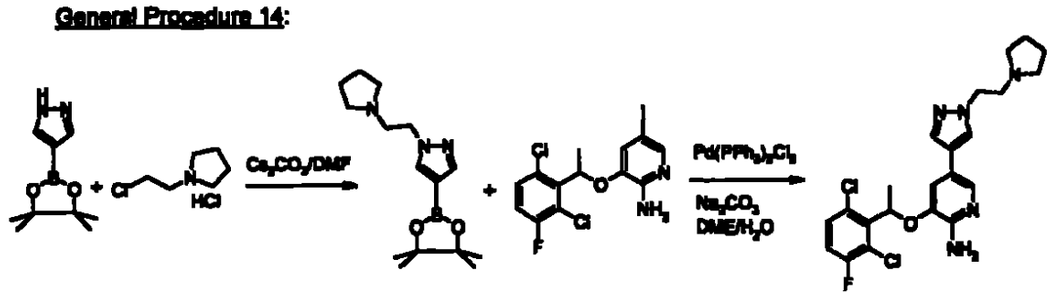
FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5475
Facsimile: (202) 672-5399

Beth A. Burrous
Attorney for Applicant
Registration No. 35,087

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File Reference: 034536/0989

IN THE INTERNATIONAL BUREAU OF WIPO

International Application Of:	:	SUGEN, INC., et al.
International Application No.	:	PCT/US2004/005495
International Filing Date :	:	26 February 2004 (26.02.2004)
Title of the Invention	:	AMINOHETEROARYL COMPOUNDS AS PROTEIN KINASE INHIBITORS

CHANGE OF ADDRESS AND ADDITION OF INVENTORS/APPLICANTS UNDER PCT RULE 92bis.4.1 (v)

Via Facsimile and Enclosures by Federal Express

International Bureau of WIPO
PCT Receiving Office Section
34, chemin des Colombettes
1211 Geneva 20
Switzerland

Attn: Idhir Britel

Sir:

Attorneys for the Applicants respectfully requests a change of address for:

1) **CUI, Jingrong Jean**
13718 Treviso Court
San Diego, CA 92130
Citizenship: US

And Addition of the following inventors/applicants for the purposes of the United States of America only:

2) **BHUMRALKAR, Dilip**
5774 Concord Woods Way
San Diego, CA 92130
United States of America
Citizenship: IN

3) **BOTROUS, Iriny**
12022 Mountain Pass Road
San Diego, CA 92128
United States of America
Citizenship: EG

4) **CHU, Ji Yu**
34740 Bowie Common
Fremont, CA 94555
United States of America
Citizenship: US

5) **FUNK, Lee A.**
5153 Mendip Street
Oceanside, CA 92057
United States of America
Citizenship: US

6) **HANAU, Cathleen Elizabeth**
15551 Wendimill Drive
Chesterfield, MO 63017
United States of America
Citizenship: US

7) **HARRIS Jr., G. Davis**
36 Shady Valley Drive
Chesterfied, MO 63017
United States of America
Citizenship: US

8) **JIA, Lei**
11895 Bridgewood Way
San Diego, CA 92128
United States of America
Citizenship: US

9) **JOHNSON, Joanne**
5 Pine Ridge Drive
Guilderland, NY 12084
United States of America
Citizenship: GB

10) **KOLODZIEJ, Stephen A.**
2448 Clarjon Drive
Ballwin, MO 63021
United States of America
Citizenship: US

11) **KUNG, Pei-Pei**
5504 Shannon Ridge Lane
San Diego, CA 92130
United States of America
Citizenship: US

12) **LI, Xiaoyuan (Sharon)**
2020 Victoria Court
Los Altas, CA 94024
United States of America
Citizenship: US

13) **LIN, Jason (Qishen)**
9670 Graceland Way
San Diego, CA 92129
United States of America
Citizenship: US

14) **MENG, Jerry Jialun**
8912 Gainsborough Avenue
San Diego, CA 92129
United States of America
Citizenship: US

15) **NAMBU, Mitchell David**
3105 Ducommun Avenue
San Diego, CA 92122
United States of America
Citizenship: US

16) **NELSON, Christopher G.**
1854 E. Fir Avenue, APT. 103
Fresno, CA 93720
United States of America
Citizenship: US

17) **PAIRISH, Mason Alan**
10996 Valldemosa Lane
San Diego, CA 92127
United States of America
Citizenship: US

18) **SHEN, Hong**
5365 Toscana Way, #428
San Diego, CA 92122
United States of America
Citizenship: CN

19) **TRAN-DUBE, Michelle**
3056 Via Alicante #P
La Jolla, CA 92037
United States of America
Citizenship: US

20) **WALTER, Allison**
137 Sugar Hill Road
Rexford, NY 12148
United States of America
Citizenship: US

21) **ZHANG, Fang-Jie**
817 Devonshire Way
Sunnyvale, CA 94087
United States of America
Citizenship: CN

22) **ZHANG, Jennifer**
1046 Gull Avenue
Foster City, CA 94404
United States of America
Citizenship: US

Copies of General Appointments of Agent for the inventors/applicants are attached with the exception of the Appointment of Agent for inventor Christopher Nelson, for which we have not received at this time.

Respectfully submitted,

Beth A. Burrous
Registration No. 35,087

Dated: 27 September 2004

Foley and Lardner LLP
Washington Harbour
3000 K Street N.W., Suite 500
Washington, DC 20007-5101

cc: United States Patent PCT Branch

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

BURROUS, Beth, A.
Foley & Lardner
Washington Harbour
3000 K Street, N.W.
Suite 500
Washington, DC 20007-5101
United States of America

Date of mailing (day/month/year) 04 November 2004 (04.11.2004)	
Applicant's or agent's file reference 034536-0989	**IMPORTANT NOTIFICATION**
International application No. PCT/US2004/005495	International filing date (day/month/year) 26 February 2004 (26.02.2004)

1. The following indications appeared on record concerning:

[X] the applicant [X] the inventor [ ] the agent [ ] the common representative

Name and Address	State of Nationality	State of Residence
	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
ZHANG, Zennifer 1046 Gull Avenue Foster City, CA 94404 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:
The person identified in box 2 should be added to the record as applicant for US only and inventor for all designated States.

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[X] the designated Offices concerned
[ ] the elected Offices concerned
[ ] other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Kinam HA
Facsimile No. (41-22) 338.70.80	Telephone No. (41-22) 338 8031

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1. The following indications appeared on record concerning:

[X] the applicant [X] the inventor [ ] the agent [ ] the common representative

Name and Address	State of Nationality	State of Residence
	CN	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
ZHANG, Fang-Jie 817 Devonshire Way Sunnyvale, CA 94087 United States of America	CN	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:
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Name and Address	State of Nationality	State of Residence
	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
WALTER, Allison 137 Sugar Hill Road Rexford, NY 12148 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:
The person identified in box 2 should be added to the record as applicant for US only and inventor for all designated States.

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PATENT COOPERATION TREATY

599

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	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
TRAN-DUBE, Michelle 3056 Via Alicante #P La Jolla, CA 92037 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

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2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

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Name and Address	State of Nationality	State of Residence
SHEN, Hong 5365 Toscana Way, #428 San Diego, CA 92122 United States of America	CN	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

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Facsimile No. (41-22) 338.70.90	Telephone No. (41-22) 338 8031

Form PCT/IB/306 (March 1994) 006494898

PATENT COOPERATION TREATY

601

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International application No.	**International filing date (day/month/year)**
PCT/US2004/005495	26 February 2004 (26.02.2004)

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Name and Address	State of Nationality	State of Residence
	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
PAIRISH, Mason Alan 10996 Valldemosa Lane San Diego, CA 92127 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:
The person identified in box 2 should be added to the record as applicant for US only and inventor for all designated States.

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[ ] other:

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Facsimile No. (41-22) 338.70.90	Telephone No. (41-22) 338 8031

PATENT COOPERATION TREATY

62

From the INTERNATIONAL BUREAU

PCT

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Foley & Lardner
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Name and Address	State of Nationality	State of Residence
	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
NELSON, Christopher G. 1854 E. Fir Avenue, Apt. 103 Fresno, CA 93720 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:

The person identified in box 2 should be added to the record as applicant for US only and inventor for all designated States.

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[X] the designated Offices concerned
[ ] the elected Offices concerned
[ ] other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Kinam HA
Facsimile No. (41-22) 338.70.90	Telephone No. (41-22) 338 8031

PATENT COOPERATION TREATY

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	Telephone No.	
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[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
NAMBU, Mitchell David 3105 Ducommun Avenue San Diego, CA 92122 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

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Facsimile No. (41-22) 338.70.90	Telephone No. (41-22) 338 8031

Form PCT/IB/308 (March 1994) 008494895

PATENT COOPERATION TREATY

GOU

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

BURROUS, Beth, A.
Foley & Lardner
Washington Harbour
3000 K Street, N.W.
Suite 500
Washington, DC 20007-5101
United States of America

Date of mailing (day/month/year)	
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International application No.	**International filing date (day/month/year)**
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[X] the applicant [X] the inventor [ ] the agent [ ] the common representative

Name and Address	State of Nationality	State of Residence
	US	US
	Telephone No.	
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2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
MENG, Jerry Jialun 8912 Gainsborough Avenue San Diego, CA 92129 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:
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Facsimile No. (41-22) 338.70.90	Telephone No. (41-22) 338 8031

PATENT COOPERATION TREATY

65

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Suite 500
Washington, DC 20007-5101
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	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
LIN, Jason(Qishen) 9670 Graceland Way San Diego, CA 92129 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

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PATENT COOPERATION TREATY

506

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[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
LI, Xiaoyuan(Sharon) 2020 Victoria Court Los Altas, CA 94024 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

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Name and Address	State of Nationality	State of Residence
KUNG, Pei-Pei 5504 Shannon Ridge Lane San Diego, CA 92130 United States of America	US	US
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United States of America

Date of mailing (day/month/year)	
04 November 2004 (04.11.2004)	
Applicant's or agent's file reference	**IMPORTANT NOTIFICATION**
034536-0989	
International application No.	**International filing date (day/month/year)**
PCT/US2004/005495	26 February 2004 (26.02.2004)

1. The following indications appeared on record concerning:

[X] the applicant [X] the inventor [ ] the agent [ ] the common representative

Name and Address	State of Nationality	State of Residence
	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
KOLODZIEJ, Stephen A. 2448 Clarion Drive Ballwin, MO 63021 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:
The person identified in box 2 should be added to the record as applicant for US only and inventor for all designated States.

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[X] the designated Offices concerned
[ ] the elected Offices concerned
[ ] other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Kinam HA
Facsimile No. (41-22) 338.70.90	Telephone No. (41-22) 338 8031

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

BURROUS, Beth, A.
Foley & Lardner
Washington Harbour
3000 K Street, N.W.
Suite 500
Washington, DC 20007-5101
United States of America

Date of mailing (day/month/year)	
04 November 2004 (04.11.2004)	
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International application No.	**International filing date (day/month/year)**
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1. The following indications appeared on record concerning:

[X] the applicant [X] the inventor [ ] the agent [ ] the common representative

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	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
JOHNSON, Joanne 5 Pine Ridge Drive Guilderland, NY 12084 United States of America	GB	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:
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[ ] the International Preliminary Examining Authority
[X] the designated Offices concerned
[ ] the elected Offices concerned
[ ] other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Kinam HA
Facsimile No. (41-22) 338.70.90	Telephone No. (41-22) 338 8031

PATENT COOPERATION TREATY

610

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

BURROUS, Beth, A.
Foley & Lardner
Washington Harbour
3000 K Street, N.W.
Suite 500
Washington, DC 20007-5101
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Date of mailing (day/month/year)	
04 November 2004 (04.11.2004)	
Applicant's or agent's file reference	**IMPORTANT NOTIFICATION**
034536-0989	
International application No.	**International filing date (day/month/year)**
PCT/US2004/005495	26 February 2004 (26.02.2004)

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Name and Address	State of Nationality	State of Residence
	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
JIA, Lei 11895 Bridgewood Way San Diego, CA 92128 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:
The person identified in box 2 should be added to the record as applicant for US only and inventor for all designated States.

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[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[X] the designated Offices concerned
[ ] the elected Offices concerned
[ ] other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Kinam HA
Facsimile No. (41-22) 338.70.80	Telephone No. (41-22) 338 8031

PATENT COOPERATION TREATY

611

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04 November 2004 (04.11.2004)	
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International application No.	**International filing date (day/month/year)**
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[X] the applicant [X] the inventor [ ] the agent [ ] the common representative

Name and Address	State of Nationality	State of Residence
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
HARRIS Jr., G. Davis 36 Shady Valley Drive Chesterfied, MO 63017 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:
The person identified in box 2 should be added to the record as applicant for US only and inventor for all designated States.

4. A copy of this notification has been sent to:

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[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[X] the designated Offices concerned
[ ] the elected Offices concerned
[ ] other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Kinam HA
Facsimile No. (41-22) 338.70.90	Telephone No. (41-22) 338 8031

PATENT COOPERATION TREATY

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Name and Address	State of Nationality	State of Residence
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
HANAU, Cathleen Elizabeth 15551 Wendimill Drive Chesterfield, MO 63017 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:
The person identified in box 2 should be added to the record as applicant for US only and inventor for all designated States.

4. A copy of this notification has been sent to:

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Facsimile No. (41-22) 338.70.90	Telephone No. (41-22) 338 8031

PATENT COOPERATION TREATY

63

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

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To:

BURROUS, Beth, A.
Foley & Lardner
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Washington, DC 20007-5101
United States of America

Date of mailing (day/month/year)	
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PCT/US2004/005495	26 February 2004 (26.02.2004)

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[X] the applicant [X] the inventor [ ] the agent [ ] the common representative

Name and Address	State of Nationality	State of Residence
	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
FUNK, Lee A. 5153 Mendip Street Oceanside, CA 92057 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:
The person identified in box 2 should be added to the record as applicant for US only and inventor for all designated States.

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PATENT COOPERATION TREATY

614

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Name and Address	State of Nationality	State of Residence
CHU, Ji Yu 34740 Bowie Common Fremont, CA 94555 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:
The person identified in box 2 should be added to the record as applicant for US only and inventor for all designated States.

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Name and Address	State of Nationality	State of Residence
BOTROUS, Iriny 12022 Mountain Pass Road San Diego, CA 92128 United States of America	EG	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:

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Name and Address	State of Nationality	State of Residence
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
CUI, Jingjong, Jean 13718 Treviso Court San Diego, CA 92130 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:
The person identified in box 2 should be added to the record as applicant for US only and inventor for all designated States.

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The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer
	Kinam HA
Facsimile No. (41-22) 338.70.90	Telephone No. (41-22) 338 8031

PATENT COOPERATION TREATY

612

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Name and Address	State of Nationality	State of Residence
CUI, Jingjong, Jean 808 Arcturus Circle Foster City, CA 94404 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[ ] the person [ ] the name [X] the address [ ] the nationality [ ] the residence

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CUI, Jingjong, Jean 13718 Treviso Court San Diego, CA 92130 United States of America	US	US
	Telephone No.	
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The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Kinam HA
Facsimile No. (41-22) 338.70.90	Telephone No. (41-22) 338 8031

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
10 September 2004 (10.09.2004)

PCT

(10) International Publication Number
WO 2004/076412 A3

(51) International Patent Classification[7]: A61K 31/4965, C07D 401/00, 403/00, 405/00, 409/00, 411/00, 413/00, 417/00, 419/00, 211/72

(21) International Application Number: PCT/US2004/005495

(22) International Filing Date: 26 February 2004 (26.02.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/449,588 26 February 2003 (26.02.2003) US
60/540,229 29 January 2004 (29.01.2004) US

(71) Applicant (*for all designated States except US*): SUGEN, INC. [US/US]; 230 East Grand Avenue, South San Francisco, CA 94080 (US).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): CUI, Jingjong, Jean [US/US]; 13718 Treviso Court, San Diego, CA 92130 (US). BHUMRALKAR, Dilip [IN/US]; 5774 Concord Woods Way, San Diego, CA 92130 (US). BOTROUS, Iriny [EG/US]; 12022 Mountain Pass Road, San Diego, CA 92128 (US). CHU, Ji Yu [US/US]; 34740 Bowie Common, Fremont, CA 94555 (US). FUNK, Lee A. [US/US]; 5153 Mendip Street, Oceanside, CA 92057 (US). HANAU, Cathleen Elizabeth [US/US]; 15551 Wendimill Drive, Chesterfield, MO 63017 (US). HARRIS Jr., G. Davis [US/US]; 36 Shady Valley Drive, Chesterfied, MO 63017 (US). JIA, Lei [US/US]; 11895 Bridgewood Way, San Diego, CA 92128 (US). JOHNSON, Joanne [GB/US]; 5 Pine Ridge Drive, Guilderland, NY 12084 (US). KOLODZIEJ, Stephen A. [US/US]; 2448 Clarjon Drive, Bullwin, MO 63021 (US). KUNG, Pei-Pei [US/US]; 5504 Shannon Ridge Lane, San Diego, CA 92130 (US). LI, Xiaoyuan(Sharon) [US/US]; 2020 Victoria Court, Los Altas, CA 94024 (US). LIN, Jason(Qishen) [US/US]; 9670 Graceland Way, San Diego, CA 92129 (US). MENG, Jerry Jiulun [US/US]; 8912 Gainsborough Avenue, San Diego, CA 92129 (US). NAMBU, Mitchell David [US/US]; 3105 Ducommun Avenue, San Diego, CA 92122 (US). NELSON, Christopher G. [US/US]; 1854 E. Fir Avenue, Apt. 103, Fresno, CA 93720 (US). PAIRISH, Mason Alan [US/US]; 10906 Valldemosa Lane, San Diego, CA 92127 (US). SHEN, Hong [CN/US]; 5365 Toscana Way, #428, San Diego, CA 92122 (US). TRAN-DUBE, Michelle [US/US]; 3056 Via Alicante #P, La Jolla, CA 92037 (US). WALTER, Allison [US/US]; 137 Sugar Hill Road, Rexford, NY 12148 (US). ZHANG, Fang-Jie [CN/US]; 817 Devonshire Way, Sunnyvale, CA 94087 (US). ZHANG, Zennifer [US/US]; 1046 Gull Avenue, Foster City, CA 94404 (US).

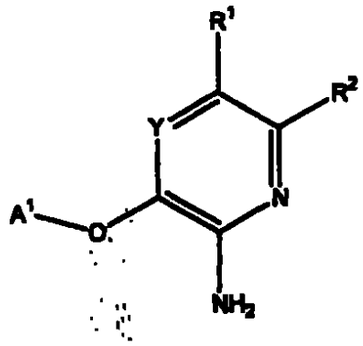
(74) Agents: BURROUS, Beth, A. et al.; Foley & Lardner, Washington Harbour, 3000 K Street, N.W., Suite 500, Washington, DC 20007-5101 (US).

(81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH,

(*Continued on next page*)

(54) Title: AMINOHETEROARYL COMPOUNDS AS PROTEIN KINASE INHIBITORS



(1)

(57) Abstract: Aminopyridine and aminopyrazine compounds of formula (1), compositions including these compounds, and methods of their use are provided. Preferred compounds of formula 1 have activity as protein kinase inhibitors, including as inhibitors of c-MET.

WO 2004/076412 A3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/05495

619

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 31/4965, 31/44; C07D 401/00, 403/00, 405/00, 409/00, 411/00, 413/00, 417/00, 419/00, 211/72

US CL : 514/255.05, 255.06, 339, 349; 544/405, 408; 546/276.7, 277.4, 280.4, 283.4, 297

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/255.05, 255.06, 339, 349; 544/405, 408; 546/276.7, 277.4, 280.4, 283.4, 297

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

STN: structure search in REGISTRY file, crossed answer set into CAPLUS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 03/000666 A1 (PFIZER PRODUCTS INC.) 03 January 2003 (03.01.2003), example at page 83, lines 27 and 28.	32-43

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 July 2004 (22.07.2004)	11 AUG 2004
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230	Authorized officer Zachary C. Tucker Telephone No. 571-272-1600

Form PCT/ISA/210 (second sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

Continuation of Box I Reason 2:
Present claims 1-31 relate to an extremely large number of possible compounds. In fact the claims contain so many options, variables and possible permutations that a lack of both clarity and conciseness within the meaning of PCT Article 6 arises to such an extent as to render a meaningful search of the claims impossible. Indeed, taking claim 1 in addition to the countless possible permutations, the claim is practically impossible to comprehend by virtue of its sheer length and complexity. These problems render it difficult, if not impossible to determine the subject-matter for which protection is sought. Consequently, the search has been carried out for those parts of the application which do appear to be clear. Thus claims 32-43 have been search fully.

621

SUPERINDUSTRIA Y COMERCIO
Radicacion : 05005226 00000000 Folios: 620
Fecha (AMD): 2005-08-26 10:50:23
Tramite : 011 PCT-PATENT 379 FASE NACI 411 PRESENTAC
Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

REQUISITOS NECESARIOS PARA PRESENTACION Y AGILIZACION DEL TRAMITE

	USUARIO	RADICADOR
PATENTE DE INVENCIÓN ✓ MODELO DE UTILIDAD	( )	( )
- Indicación de que se solicita la concesión de una patente ✓	( )	( )
- Datos de identificación del solicitante o de la persona que se presenta la solicitud ✓	( )	( )
- Descripción de la invención. ✓	( )	( )
- Dibujos de ser estos pertinentes.	( )	( )
- Comprobante de Pago de las tasas establecidas ✓		
COMPLETA ( ) INCOMPLETA	( )	( )
DISEÑO INDUSTRIAL ( )		
- Indicación de que se solicita el registro de Diseño Industrial	( )	( )
- Datos de identificación del solicitante o de la persona que presenta	( )	( )
- la solicitud.		
- Representación gráfica o fotográfica del Diseño Industrial o muestra del Material que incorpora el diseño.	( )	( )
Comprobante de pago de las tasas establecidas	( )	( )
COMPLETA ( ) INCOMPLETA	( )	( )
ESQUEMA DE TRAZADO ( )		
- Indicación de que solicita el registro de un Esquema de trazado.	( )	( )
- Datos de identificación del solicitante o de la persona que presenta La solicitud.	( )	( )
Representación gráfica del esquema de trazado	( )	( )
Comprobante de pago de las tasas establecidas.	( )	( )
COMPLETA ( ) INCOMPLETA	( )	( )

Firma Responsable:

Fecha: agosto 26 de 2005

REPUBLICA DE COLOMBIA

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

622

Bogotá,
2020

Doctor(a)
OLARTE GARCIA CARLOS REINALDO

REFERENCIA	**Radicación No.**	**5 85226**
	Solicitud internacional	**US2004/005495**
	Fecha inicio fase nacional	**26/09/2005**
	Trámite	**11**
	Evento	**379**
	Actuación	**430**
	Oficio No.	**009742**

Como resultado del examen de forma, realizado con fundamento en el artículo 38 de la Decisión 486 de la Comisión de la Comunidad Andina, artículo 27 del Tratado de Cooperación en Materia de Patentes (PCT), regla 51 bis del Reglamento y Circular Única de la Superintendencia de Industria y Comercio, se le comunica que:

1. La solicitud no contiene la copia del documento en que consta la cesión del derecho a la patente del inventor al solicitante o a su causante. (Art. 26-k) Decisión 486.

2. Aclarar el motivo por el cual el Señor J. Trevor Lumb aparece con diferentes cargos en distintas compañías: Secretario Asistente con Pharmacia & Upjohn Company, Vicepresidente con Pfizer Products Inc, Asistente General Consejero de Patentes en Pfizer Inc, Secretario Asistente con Warner Lambert Company LLC.

En cumplimiento de lo dispuesto por el artículo 39 de la Decisión 486, se le requiere para que dentro del término de dos meses siguientes a la fecha de notificación del presente oficio, complete los requisitos anteriormente enunciados. En caso de no dar cumplimiento al presente requerimiento, la solicitud se considerará abandonada y perderá su prelación.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Unica No.10 de 2001.

ALIX CARMENZA CESPEDES DE VERGEL
Jefe de la división de Nuevas Creaciones

El anterior requerimiento fue notificado por fijación en lista de fecha 21 OCT. 20[illegible]
adpal