SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
INVENTARIO

CSA047345

Organizacion y
Digitalizacion CSA Ltda

Industria y Comercio

SUPERINTENDENCIA

PCT

DELEGATURA DE PROPIEDAD INDUSTRIAL

DIVISIÓN DE NUEVAS CREACIONES

08-24630

SOLICITUD DE PATENTE DE INVENCIÓN

TITULO: COMPUESTOS DE IMIDAZOL PARA EL TRATAMIENTO DE TRASTORNOS NEUROLÓGICOS

SOLICITANTE: PFIZER PRODUCTS INC.

DIRECCIÓN: EASTERN POINT ROAD, GROTON, CONNECTICUT 06340 E.U.A

A61K 31/4178

APODERADO: CARLOS R. OLARTE

BOGOTÁ 07 de Marzo de 2008

202099

P2008/000036

55

OLARTERAISBECK

Industria y Comercio
SUPERINTENDENCIA

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
No. 08-024630- -00000-0000
Fecha: 2008-03-07 16:56:05 Dep. 2020 NUECREACIONI
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 411 PRESENTACION Folios: 440

PETITORIO - FORMULARIO [illegible] DE SOLICITUD
PATENTE PCT
ENTRADA EN FASE NACIONAL **P2008/000036**

SOLICITUD DE:

(1) [X] Patente de Invención. [ ] Patente de Modelo de Utilidad.

[X] Capítulo I. [ ] Capítulo II.

(2) **SOLICITANTE (71)**

Nombre: PFIZER PRODUCTS INC.
Dirección: Eastern Point Road, Groton, CT 06340, E.U.A.
Nacionalidad o Domicilio: ESTADOUNIDENSE
Lugar de Constitución: Estados Unidos de América.
Teléfono: _____ **Fax:** _____
E-mail: _____

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

REPRESENTANTE O APODERADO

Nombre: CARLOS R. OLARTE
Dirección: World Trade Center Torre A, Calle 100 No. 8A-37 Piso 10
Teléfono: 601-7700 **Fax:** 601-7799
E-mail: office@olarteraisbeck.com

IDENTIFICACIÓN
C.C. [X] **NIT** [ ]
C.E. [ ] **Otro** [ ]
Cual _____
Número 79782747Bta
TP 74.295

INVENTOR (ES) (72)

Nombre: VER PAGINA DJUNTA
Dirección: VER PAGINA ADJUNTA
Nacionalidad o Domicilio: VER PAGINA ADJUNTA

(5) **PCT (86)**

Solicitud Internacional No. PCT/IB2006/002753 Fecha Septiembre 11, 2006

Publicación Internacional No. WO 2007/034326 Fecha Marzo 29, 2007

(6) **Título (54)** **COMPUESTOS DE IMIDAZOL PARA EL TRATAMIENTO DE TRASTORNOS NEUROLÓGICOS**

Clasificación Internacional (51) C07D 233/54, C07D 401/04, C07D 403/04, C07D 403/10, C07D 403/12, C07D 401/12, C07D 405/12, C07D 405/06, C07S 401/06, C07D 409/12, C07D 413/12, C07D 487/04, C07D 487/08, A61K 31/4178

A61P 25/00

Prioridad

SI [X] **NO** [ ]

(33) País de Origen	(32) Fecha	(31) Número de Solicitud
US	Septiembre 22, 2005	60/719,521

(9) **Comprobante de pago No.** 08 – 16,715 **Fecha** Febrero 26,, 2008

(0) **ANEXOS**

2

- [x] Comprobante de pago de la tasa de presentación de la solicitud.
- [x] Documento que acredita la existencia y representación legal cuando el solicitante sea persona jurídica.
- [x] Poderes, si fuere el caso. Adjunto Copia simple. Ver expediente No. 06-033.245.
- [x] 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).
- [ ] Copia del examen preliminar internacional efectuado por la Autoridad Internacional de Examen Preliminar (IPEA).
- [ ] 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.
- [ ] De ser el caso, modificaciones efectuadas a la solicitud internacional.
- [x] Otros. Búsqueda Internacional

(1) **FIGURA CARACTERÍSTICA:**

(2) 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.

LISTA DE INVENTORES **PCT/IB2006/002753**

1- **MICHAEL AARON BRODNEY,**
Eastern Point Road, Groton,
CT 06340
Estados Unidos
Nacionalidad: Estadounidense

2. **YUHPYNG LIANG CHEN,**
Eastern Point Road, Groton,
CT 06340
Estados Unidos
Nacionalidad: Estadounidense

3. **KAREN JEAN COFFMAN,**
Eastern Point Road, Groton,
CT 06340
Estados Unidos
Nacionalidad: Estadounidense

4. **EDWARD FOX KLEINMAN,**
Eastern Point Road, Groton,
CT 06340
Estados Unidos
Nacionalidad: Estadounidense

5. **BRIAN THOMAS O'NEILL,**
Eastern Point Road, Groton,
CT 06340
Estados Unidos
Nacionalidad: Estadounidense

36

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2

RECIBO OFICIAL DE CAJA : 08 - 16,715
FECHA : FEBRERO 26 DE 2008

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
No. 08-024630- -00000-0000
Fecha. 2008-03-07 16:56:05 Dep. 2020 NUECREACIONI
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 411 PRESENTACION Folios: 440

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

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
OLARTE RAISBECK	CONSIGNACION	BANCO DE BOGOTA	062754387	1483223	26/02/2008	4,404,000.00

***** 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	501,000.00
			TOTAL : $	501,000.00

SON: QUINIENTOS UN MIL PESOS

RESPONSABLE : _____

RECIBO DE CAJA APLICADO AL EXPEDIENTE No._____

6

TRADUCCION OFICIAL No. 05-223

Efectuada el día 9 de diciembre de 2005, de un documento escrito en Inglés, al cual para su identificación se le estampa el sello de Sergio Andrés Rueda Iglesias, Traductor e Intérprete Oficial por Resolución No. 0138 expedida por el Ministerio de Justicia y del Derecho el 11 de febrero de 2002.

Traducción de las Autenticaciones Notariales y subsiguientes correspondientes a un Poder otorgado por **PFIZER PRODUCTS, INC.**, a **Carlos R. Olarte y/o J. Ian Raisbeck y/o Ana María Frieri y/o Juan Guillermo Moure y/o Natalia Castro,** documento este que viene en español, se explica por sí solo y fue firmado por Grover F. Fuller, Jr. el 17 de noviembre de 2005 en Nueva York, Estados Unidos de América.

También en inglés y en español viene Certificación Notarial mediante la cual se confirma el nombre y cargo de **Grover F. Fuller, Jr,** así como la existencia legal de la compañía. Dicha certificación notarial está firmada por Susan Z. Killian, Notario Público de Nueva York, cuyo cargo expira el 4 de octubre de 2008, según consta en su correspondiente sello notarial.

Suscrito y jurado ante mi el 17 de noviembre de 2005.

(Fdo.) Susan Z. Killian

SERGIO ANDRES RUEDA IGLESIAS
C. C. [illegible]
TRADUCTOR E INTERPRETE OFICIAL
ESPAÑOL - INGLES - ESPAÑOL
RESOLUCION No. 0138 DEL 11.2002
MINISTERIO DE JUSTICIA Y DEL DERECHO

6

ESTADO DE NUEVA YORK - CONDADO DE NUEVA YORK No. 467518

El suscrito, Norman Goodman, Escribano del Condado y del Tribunal Supremo del Estado de Nueva York, tribunal éste provisto de sello por ley, por medio de este documento certifico conforme a la ley ejecutiva del Estado de Nueva York que Susan Z. Killian, cuyo nombre aparece suscrito en la declaración jurada o certificado de reconocimiento anexo, desempeñaba en el momento de tomar el mismo, las funciones de Notario Público, en y para el Estado de Nueva York, estando debidamente comisionado bajo juramento y habilitado como tal; que conforme a la ley en mi despacho obra un certificado de su nombramiento con su firma autógrafa; que conozco bien la letra manuscrita de dicho Notario Público o he comparado la firma que aparece en el instrumento anexo con la que reposa en los archivos de mi oficina, y creo en conciencia que la misma es auténtica.

EN FE DE LO CUAL, firmo de mi puño y letra y estampo mi sello oficial, el día 22 de noviembre de 2005.

(Fdo.) Norman Goodman, Escribano del Condado y del Tribunal Supremo del Estado de Nueva York.

SERGIO ANDRES RUEDA IGLESIAS
C. C. [illegible] 773
TRADUCTOR E INTERPRETE OFICIAL
ESPAÑOL - INGLES / INGLES - ESPAÑOL
RESOLUCION No. 0138 DE FEBRERO 11 2002
MINISTERIO DE JUSTICIA Y DEL DERECHO

7

APOSTILLA

(Convención de La Haya del 5 de octubre de 1961)

1. País: Estados Unidos de América

   El presente documento público

2. Fue firmado por: Norman Goodman

3. Que actuó en su calidad de: Escribano del Condado

4. Lleva el sello del Condado de Nueva York

   Se certificó:

5. En Nueva York, Nueva York

6. El 22 de noviembre de 2005

7. Por parte del Secretario de Estado, (Encargado) del Estado de Nueva York

8. Bajo el Número **NYC-10404952A**

9. Aparece Sello del Estado de Nueva York

10. Firmado por: James Bizzarri, Secretario de Estado Especial Encargado

Es traducción fiel y completa efectuada por:

Sergio Andrés Rueda Iglesias
c.c. 80.424.773 de Bogotá

SERGIO ANDRES RUEDA IGLESIAS
C. C. 80.424.773 DE BOGOTA
TRADUCTOR E INTERPRETE OFICIAL
ESPAÑOL - INGLES / INGLES - ESPAÑOL
RESOLUCION NO. 0783 DE FEBRERO 11 2002
MINISTERIO DE JUSTICIA Y DEL DERECHO

Apostille

(Convention de La Haye du 5 Octobre 1961)

B

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 22nd day of November 2005

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

8. No. NYC-10404952A

9. Seal/Stamp 10. Signature

James Bizzarri
Special Deputy Secretary of State

COLOMBIA

OLARTERAISBECK
OLARTE RAISBECK & FRIERI LTDA.

Carlos R. Olarte
J. Ian Raisbeck
Ana María Frieri
Juan Guillermo Moure
Natalia Castro

Zayde Chahin
Zaava Ravid
Jacqueline Chaparro
Jose Luis Londoño
Camilo Alvarez
Felipe Mendoza
Camilo Rodríguez
Santiago Pardo

Of Counsel
Guillermo Chahín
Graciela Melo

Power of Attorney

Poder

The undersigned,

El suscrito,

PFIZER PRODUCTS INC.,

domiciled in

domiciliado en

Eastern Point Road, Groton, State of Connecticut 06340, United States of America

by means of these presents hereby grants to **Carlos R. Olarte and/or J. Ian Raisbeck and/or Ana María Frieri and/or Juan Guillermo Moure and/or Natalia Castro** full and sufficient Power of Attorney to file, prosecute, obtain, defend and enforce any and all of the company's **Patents for Inventions, Utility Models, Layout-Designs (topographies) of Integrated Circuits, Industrial Designs, Trademarks, Advertising Slogans, Trade Names, Commercial Emblems, Geographical Indications, Protection of Trade Secrets, Obtainer's Certificates, Copyrights, Registration of Domain Names, Health Registrations, or any other intellectual property right** 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, recourses, 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 J. Ian Raisbeck y/o Ana María Frieri y/o Juan Guillermo Moure y/o Natalia Castro** poder especial, amplio y suficiente para presentar, tramitar, obtener, defender y hacer respetar todas y cualquiera de las **Patentes de Invención, Modelos de Utilidad, Esquemas de Trazados de Circuitos Integrados, Diseños Industriales, Marcas, Lemas Comerciales, Nombres Comerciales, Enseñas Comerciales, Denominaciones de Origen, Protección de Secretos Empresariales, Certificados de Obtentor, Derechos de Autor, Registro de Nombres de Dominio, Registros Sanitarios, o cualquier otro bien de propiedad intelectual** 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, recursos, 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.

PFIZER PRODUCTS INC.,

Signature/Firma:

By: Grover F. Fuller, Jr.
Vice President, Attorney-In- Fact

Date/Fecha: 17 November 2005

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

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Notarial Certification

On this date,

The undersigned Notary Public certifies:

1. That

Grover F. Fuller, Jr.

of legal age and domiciled in

Street 150 East 42nd Street
City New York
State New York 10017-5612 USA

signed the foregoing document.

2. That the grantor has executed the foregoing document as Vice President, Attorney-In-Fact of **PFIZER PRODUCTS INC.**

3. That **PFIZER PRODUCTS INC,** having its principal place of business located in Groton, State of Connecticut 06340, United States of America 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.

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 legitima.

NOTARY PUBLIC (Signature): Susan Z. Killian

SUSAN Z. KILLIAN
Notary Public, State of New York
No. 01KI6116521
Qualified in New York County
Commission Expires October 4, 2008

State of New York)
County of New York)
SWORN to and SUBSCRIBED before me
this 17 day of Nov. 2005
Susan Z. Killian

APOSTILLA

(Convención de la Haya del 5 de Octubre de 1961)

1. País: Estados Unidos de América

2. El presente documento público fue firmado por: BRIAN JACKSON, JR.

3. Que actuó en su calidad de Notario Público en y para El Distrito de Columbia.

4. Y lleva el sello del Notario

Público BRIAN JACKSON. JR.,

Se certifico

5. En Washington, D.C

6. El 18 de enero de 2008

7. Por el secretario de Distrito de Columbia.

8. Bajo el Número **185936**. Lleva el Sello.

10. Firmado por Stefhanie D. Scott, Secretario de Estado

12

CESION

Para la valiosa consideración pagada por mi (nosotros) by PFIZER PRODUCTS INC. una corporación organizada bajo las leyes del estado de Connecticut, Estados Unidos de América que es dirección completa de la oficina de correos Eastern Point Road, Groton, Connecticut 06340, Estados Unidos de América, Yo (nosotros) vende y asigna por este medio a PFIZER PRODUCTS INC, toda mi (nuestra) derecha, titulo e interés en y para mi (nuestro) invención para una nueva y útil mejora dentro de "COMPUESTOS DE IMIDAZOL PARA EL TRATAMIENTO DE TRASTORNOS NEUROLÓGICOS" cuanto la Republica de Colombia se refiere, como completamente dispuesto descrito en la especificación yo (nosotros) autoriza por este medio a comisión de patentes de Colombia a publicar la patente dicha a PFIZER PRODUCTS INC de acuerdo a esta cesion.

Dando fe yo (nosotros) tiene

(firma ilegible) Michael Aaron BRODNEY
Groton, CT, USA 10 de Julio de 2006 – Michael Aaron BRODNEY

(firma ilegible) Yuhping Liang CHEN
Groton, CT, USA 10 de Julio de 2006 – Yuhping Liang CHEN

(firma ilegible) Karen Jean KOFFMAN
Groton, CT, USA 10 de Julio de 2006 – Karen Jean KOFFMAN

(firma ilegible) Edward Fox KLEINMAN
Groton, CT, USA 10 de Julio de 2006– Edward Fox KLEINMAN

(firma ilegible) Brian Thomas O´NEILL
Groton, CT, USA 10 de Julio de 2006– Brian Thomas O´NEILL

P2008/000036

13

Apostille

(Convention de La Haye du 5 octobre 1961)

1. *District of Columbia*
   United States of America
2. This public document has been signed by BRIAN JACKSON, JR.
3. acting in the capacity of NOTARY PUBLIC IN AND FOR THE DISTRICT ~~OF COLUMBIA~~
4. bears the seal/stamp of BRIAN JACKSON, JR., NOTARY PUBLIC, D.C.

CERTIFIED

5. at Washington, D.C.
6. the 18TH day of JANUARY 2008
7. by *Secretary of the District of Columbia*
8. No. 185936
9. Seal/S

86 - PO138

10. Signature

STEPHANIE D. SCOTT

PC33065A

CO-1

ASSIGNMENT

19

For valuable consideration paid to me (us) by **PFIZER PRODUCTS INC.** a corporation organized under the laws of **the State of Connecticut, United States of America** whose full post office address is **Eastern Point Road, Groton, Connecticut 06340, United States of America**, I (we) do hereby sell and assign to the said **PFIZER PRODUCTS INC.**, all my (our) right, title and interest in and to my (our) invention for a new and useful Improvement in **IMIDAZOLE COMPOUNDS FOR THE TREATMENT OF NEUROLOGICAL DISORDERS** so far as the Republic of Colombia is concerned, as fully set forth and described in the specification, and I (we) do hereby authorize and request the Commissioner of Patents of Colombia to issue said patent to the said **PFIZER PRODUCTS INC.** in accordance with this assignment.

In witness whereof I (we) have hereunto set my (our) hand(s) this

Place, date and signature - Michael Aaron BRODNEY

GROTON, CT JUL 10 2006 USA

Place, date and signature - Yuhpyng Liang CHEN

GROTON, CT JUL 10 2006 USA

Place, date and signature - Karen Jean COFFMAN

GROTON, CT JUL 10 2006 USA

Place, date and signature - Edward Fox KLEINMAN

GROTON, CT JUL 10 2006 USA

Place, date and signature - Brian Thomas O'NEILL

I HEREBY CERTIFY THAT THIS
IS THE ORIGINAL DOCUMENT

District of Columbia: SS
Subscribed and Sworn to before me
this 18th day of January, 20 01

Brian Jackson, Jr. Notary Public, D.C.
My Commission Expires February 29, 2012

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
29 March 2007 (29.03.2007)

PCT

(10) International Publication Number
WO 2007/034326 A2

(51) International Patent Classification:
C07D 233/54 (2006.01) *C07D 403/04* (2006.01)
C07D 401/04 (2006.01) *C07D 403/10* (2006.01)

(21) International Application Number:
PCT/IB2006/002753

(22) International Filing Date:
11 September 2006 (11.09.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/719,521 22 September 2005 (22.09.2005) US

(71) Applicant *(for all designated States except US)*: **PFIZER PRODUCTS INC.** [US/US]; Eastern Point Road, Groton, CT 06340 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **BRODNEY, Michael, Aaron** [US/US]; Pfizer Global Research and Development, Eastern Point Road, Groton, CT 06340 (US). **CHEN, Yuhpyng, Liang** [US/US]; Pfizer Global Research and Development, Eastern Point Road, Groton, CT 06340 (US). **COFFMAN, Karen, Jean** [US/US]; Pfizer Global Research and Development, Eastern Point Road, Groton, CT 06340 (US). **KLEINMAN, Edward, Fox** [US/US]; Pfizer Global Research and Development, Eastern Point Road, Groton, CT 06340 (US). **O'NEILL, Brian, Thomas** [US/US]; Pfizer Global Research and Development, Eastern Point Road, Groton, CT 06340 (US).

(74) Agent: **FULLER, Grover, F., Jr.**; c/o LAWRENCE, Jackie, Pfizer Inc. MS8260-1615, Eastern Point Road, Groton, CT 06340 (US).

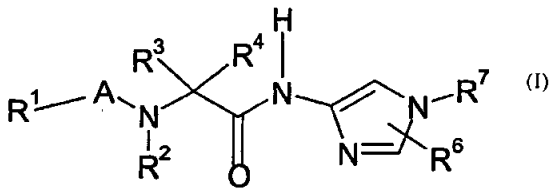
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ,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

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, 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, IS, IT, LT, LU, LV, MC, NL, PL, 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: IMIDAZOLE COMPOUNDS FOR THE TREATMENT OF NEUROLOGICAL DISORDERS



(I)

(57) Abstract: The present invention relates to compounds of Formula (I) wherein R^1, R^2, R^3, R^4, R^6, R^7 and A are as defined. Compounds of Formula (I) have activity inhibiting production of Aβ-peptide. The invention also relates to pharmaceutical compositions and methods for treating diseases and disorders, for example, neurodegenerative and/or neurological disorders, e.g., Alzheimer's disease, in a mammal comprising compounds of Formula (I).

WO 2007/034326 A2

IMIDAZOLE COMPOUNDS FOR THE TREATMENT OF NEUROLOGICAL DISORDERS

Field of the Invention

The present invention relates to the treatment of neurodegenerative and/or neurological disorders, such as Alzheimer's disease, in mammals, including humans. This invention also relates to inhibiting, in mammals, including humans, the production of Aβ-peptides that can contribute to the formation of neurological deposits of amyloid protein. More particularly, this invention relates to imidazole compounds, pharmaceutical compositions comprising such compounds and methods of using such compounds, *i.e.*, for the treatment of neurodegenerative and/or neurological disorders, such as Alzheimer's disease, related to Aβ-peptide production.

Background of the Invention

Dementia results from a wide variety of distinctive pathological processes. The most common pathological processes causing dementia are Alzheimer's disease (AD), cerebral amyloid angiopathy (CAA) and prion-mediated diseases. AD affects nearly half of all people past the age of 85, the most rapidly growing portion of the United States population. As such, the number of AD patients in the United States is expected to increase from about 4 million to about 14 million by the middle of the next century.

Treatment of AD typically is the support provided by a family member in attendance. Stimulated memory exercises on a regular basis have been shown to slow, but not stop, memory loss. A few drugs, for example Aricept™, provide treatment of AD.

A hallmark of AD is the accumulation in the brain of extracellular insoluble deposits called amyloid plaques and abnormal lesions within neuronal cells called neurofibrillary tangles. Increased plaque formation is associated with an increased risk of AD. Indeed, the presence of amyloid plaques, together with neurofibrillary tangles, is the basis for definitive pathological diagnosis of AD.

The major components of amyloid plaques are the amyloid Aβ-peptides, also called Aβ-peptides, that consist of several proteins including 38, 40, 42 or 43 amino acids, designated as the $A\beta_{1-38}$, $A\beta_{1-40}$, $A\beta_{1-42}$ and $A\beta_{1-43}$ peptides, respectively. The Aβ-peptides are thought to cause nerve cell destruction, in part, because they are toxic to neurons in vitro and in vivo.

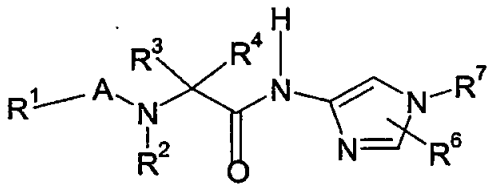
The Aβ peptides are derived from larger amyloid precursor proteins (APP proteins), that consist of four proteins containing 695, 714, 751 or 771 amino acids, designated as the APP_{695}, APP_{714}, APP_{751} and APP_{771}, respectively. Proteases are believed to produce the Aβ peptides by cleaving specific amino acid sequences within the various APP proteins. The proteases are named "secretases" because the Aβ-peptides they produce are secreted by cells into the extracellular environment. These secretases are each named according to the cleavage(s) they make to produce the Aβ-peptides. The secretase that forms the amino

terminal end of the Aβ-peptides is called the beta-secretase. The secretase that forms the carboxyl terminal end of the Aβ-peptides is called the gamma-secretase.

This invention relates to novel compounds that inhibit Aβ-peptide production, to pharmaceutical compositions comprising such compounds, and to methods of using such compounds to treat neurodegenerative and/or neurological disorders.

Summary of the Invention

The present invention relates to compounds of Formula I



I

wherein R^1, R^2, R^3, R^4, R^6, R^7 and A are as defined below. Compounds of Formula I have activity inhibiting production of Aβ-peptide. The invention also relates to pharmaceutical compositions and methods for treating diseases and disorders, for example, neurodegenerative and/or neurological disorders, *e.g.*, Alzheimer's disease, in a mammal comprising compounds of Formula I.

Detailed Description of the Invention

In one embodiment, the present invention relates to compounds of Formula I

wherein A is absent or is selected from  -C- , -N-C-, -Z-C-, -Z-C- and SO_2;

Z is selected from $-CH_2$, $-CH(OH)$, $-CH(C_1\text{-}C_6$ alkyl), $-CH(C_1\text{-}C_6$ alkoxy), $-CH(NR^9R^{10})$, $-CH(CH_2(OH))$, $-CH(CH(C_1\text{-}C_4$ alkyl)(OH)) and $-CH(C(C_1\text{-}C_4$ alkyl)($C_1\text{-}C_4$alkyl)(OH));

R^1 is selected from $-C_1\text{-}C_{20}$ alkyl, $-C_2\text{-}C_{20}$ alkenyl, $-C_2\text{-}C_{20}$ alkynyl, $-C_1\text{-}C_{20}$ alkoxy, $-C_2\text{-}C_{20}$ alkenoxy, $-C_1\text{-}C_{20}$ hydroxyalkyl, $-C_3\text{-}C_8$ cycloalkyl, benzo($C_3\text{-}C_8$ cycloalkyl), benzo($C_3\text{-}C_8$ heterocycloalkyl), $-C_4\text{-}C_8$ cycloalkenyl, -($C_5\text{-}C_{11}$)bi- or tricycloalkyl, benzo($C_5\text{-}C_{11}$)bi- or tricycloalkyl, ($C_7\text{-}C_{11}$)bi- or tricycloalkenyl, (3-8 membered) heterocycloalkyl, $-C_6\text{-}C_{14}$ aryl and (5-14 membered) heteroaryl, wherein R^1 is optionally substituted by R^{1a};

wherein R^{1a} in each instance is independently selected from –OH, halo, $-C_1\text{-}C_6$ alkoxy, -CN, $-NO_2$, $-NR^9R^{10}$, $-C(=O)NR^9R^{10}$, $-C(=O)R^{11}$, $-C(=O)OR^{12}$, $-SO_2\text{-}NR^9R^{10}$, $-S(O)_n\text{-}R^{11}$, $-C_3\text{-}C_{15}$ cycloalkyl, $-C_4\text{-}C_{15}$ cycloalkenyl, -($C_5\text{-}C_{11}$)bi- or tricycloalkyl, -($C_7\text{-}C_{11}$)bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, $-C_6\text{-}C_{15}$ aryl, -(5-15 membered) heteroaryl, $-C_6\text{-}C_{15}$ aryloxy and -(5-15 membered) heteroaryloxy;

wherein said alkoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{1a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{1b};

wherein R^{1b} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

R^2 is selected from H, -C_1-C_8 alkyl, -C_2-C_8 alkenyl, -C_3-C_8 cycloalkyl and -C_3-C_8 cycloalkenyl, wherein R^2 is optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkyl optionally substituted with from one to three halo atoms, -C_1-C_4 alkoxy optionally substituted with from one to three halo atoms, halo and -OH;

or R^1 and R^2 together with the A group when present and the nitrogen atom to which R^2 is attached, or R^1 and R^2 together with the nitrogen atom to which R^1 and R^2 are attached when A is absent, may optionally form a four to eight membered ring;

R^3 is selected from H, -C_1-C_8 alkyl, -C_2-C_8 alkenyl, -C_2-C_8 alkynyl, -C_3-C_8 cycloalkyl,-C_5-C_8 cycloalkenyl and (3-8 membered) heterocycloalkyl, -C_6-C_{14} aryl and -(5-14 membered) heteroaryl, wherein said alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, aryl or heteroaryl are each optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkoxy, halo, -OH, -S(C_1-C_4)alkyl, -C_1-C_4 alkyl -C(=O)OR^9, -SO_2R^9 and -(3-8 membered) heterocycloalkyl wherein said alkyl, alkoxy, and heterocyloalkyl may be further substituted by one to six halo;

R^4 is H,-C_1-C_8 alkyl or halo;

or R^3 and R^4 may together with the carbon atom to which they are attached optionally form a moiety selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, morpholino, piperidino, pyrrolidino, tetrahydrofuranyl and perhydro-2H-pyran, wherein said moiety formed by R^3 and R^4 is optionally substituted with from one to three substituents independently selected from -C_1-C_8 alkyl optionally substituted with from one to three halo atoms, -C_1-C_8 alkoxy optionally substituted with from one to three halo atoms, halo, -OH, -CN and allyl;

R^6 is selected from H, -C_1-C_8 alkyl, -C_2-C_8 alkylene, -C_1-C_8 alkoxy, halo, -CN, -C_3-C_{12} cycloalkyl ,-C_4-C_{12} cycloalkenyl (5-10 membered) heteroaryl and -C_6-C_{10} aryl, wherein said alkyl, alkylene and alkoxy of R^6 are each optionally independently substituted with from one to three substituents independently selected from halo and –CN, and wherein said cycloalkyl, cycloalkenyl, heteroaryl and aryl of R^6 are each optionally independently substituted with from

one to three substituents independently selected from -C_1-C_4 alkyl optionally substituted with from one to three halo atoms, -C_1-C_4 alkoxy optionally substituted with from one to three halo atoms, halo and –CN;

R^7 is -C_1-C_{20} alkyl substituted by -C_3-C_{12} cycloalkyl, -C_4-C_{12} cycloalkenyl, -(C_5-C_{20}) bi- or tricycloalkyl, -(C_7-C_{20})bi- or tricycloalkenyl, -(3-12 membered) heterocycloalkyl, -(7-20 membered) heterobi- or heterotricycloalkyl, -C_6-C_{14} aryl, benzo(C_3-C_8 heterocycloalkyl), -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy, wherein R^7 is independently substituted with from one to six substituents independently selected from R^{7a};

or R^7 is -C_3-C_{20} cycloalkyl, -C_4-C_{12} cycloalkenyl, -(C_5-C_{20}) bi- or tricycloalkyl, -(C_7-C_{20})bi- or tricycloalkenyl, -(3-12 membered) heterocycloalkyl, -(7-20 membered) heterobi- or heterotricycloalkyl, -C_6-C_{14} aryl, benzo(C_3-C_8 cycloalkyl), -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy substituted by at least one -C_1-C_{20} alkyl, wherein said cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, heterobi- or heterotricycloalkyl, aryl, benzocycloalkyl, heteroaryl, aryloxy and heteroaryloxy is optionally independently substituted with from one to six substituents independently selected from R^{7a}; and wherein said alkyl is substituted by R^{7C};

wherein R^{7a} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl, -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy; wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenoxy, alkynoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{7a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{7b};

wherein R^{7b} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl, -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

wherein R^{7C} in each instance is independently selected from -C_1-C_6 alkoxy, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy; wherein said alkenoxy, cycloalkyl, cycloalkenyl, bi- or

tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{7c} are each optionally independently substituted with from one to six substituents independently selected from the group R^{7b};

or R^6 and R^7 may together with the carbon and nitrogen atoms to which they are respectively attached optionally form a -(5-8 membered) heterocycloalkyl ring, a -(5-8 membered) heterocycloalkenyl ring or a -(6-8 membered) heteroaryl ring, wherein said heterocycloalkyl, heterocycloalkenyl and heteroaryl rings are each optionally independently substituted with from one to three substituents independently selected from halo,-C_1-C_6 alkyl, optionally subsituted with from one to three halo atoms, -C_1-C_6 alkoxy optionally subsituted with from one to three halo atoms, -C_1-C_6 hydroxyalkyl, -OH, -$(CH_2)_{zero\text{-}10}NR^9R^{10}$, -$(CH_2)_{zero\text{-}10}C(=O)NR^9R^{10}$, -$SO_2NR^9R^{10}$ and -C_3-C_{12} cycloalkyl;

R^9 and R^{10} in each instance are each independently selected from H, -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy, wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenoxy, alkynoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^9 of R^{10} are each optionally independently substituted with from one to six substituents independently selected from the group R^{10a};

wherein R^{10a} in each instance is independently selected from –OH, halo, -C_1-C_{12} hydroxyalkyl, -C_1-C_6 alkoxy, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_nR^{11}$, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy; wherein said alkoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{10a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{10b};

wherein R^{10b} in each instance is independently selected from -OH, halo; -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_nR^{11}$, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

or NR^9R^{10} may form a (4-20 membered) heterocycloalkyl, (5-18 membered) heterobi- or tricycloalkyl (5-18 membered) heterobi- or tricycloalkenyl, or -(5-15 membered) heteroaryl,

wherein said heterocycloalkyl, heterobi- or tricycloalkyl, heterobi- or tricycloalkenyl or heteroaryl are optionally independently substituted with from one to six substituents independently selected from-C_1-C_6 alkyl,-C_2-C_6 alkenyl,-C_2-C_6 alkenyl,-C_1-C_6 alkoxy,-C_2-C_6 alkenoxy,-C_2-C_6 alkynoxy,-C_1-C_6 hydroxyalkyl,-C_2-C_8 hydroxyalkenyl,-C_2-C_6 hydroxyalkenyl, halo, -OH, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$-$C(=O)R^{11}$, -$C(=O)OR^{11}$, -$S(O)_nR^{11}$ and -$S(O)_n$-$NR^{11}R^{12}$;

R^{11} and R^{12} in each instance are each independently selected from H, -C_1-C_8 alkyl, -C_3-C_8 cycloalkyl, -C_4-C_8 cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, (3-8 membered) heterocycloalkyl,-C_6-C_{10} aryl and -(5-14 membered) heteroaryl, wherein said alkyl of R^{11} is optionally independently substituted with from one to three substituents independently selected from –OH, -CN and -C_3-C_8 cycloalkyl, and wherein each hydrogen atom of said alkyl is optionally independently replaced with a halo atom, and wherein said cylcoalkyl, cycloalkenyl, heterocycloalkyl, aryl and hetereoaryl of R^{11} are each optionally independently substituted with from one to three substituents independently selected from halo, -C_1-C_8 alkyl optionally substituted with from one to three halo atoms, -OH, -CN and -C_3-C_8 cycloalkyl; and

n is in each instance an integer independently selected from zero, 1 and 2;

or a pharmaceutically acceptable salt thereof.

In one aspect of the above embodiment, R^7 is a -C_4-C_8 cycloalkyl, -(4-10 membered) heterocycloalkyl, -C_6-C_{14} aryl or -(5-15 membered) heteroaryl substituted by a -C_1-C_4 alkyl and wherein said alkyl is further substituted by R^{7C}, wherein R^{7C} is –NR^9R^{10}.

In another aspect of the above embodiment, R^9 is hydrogen or methyl, R^{10} is -C_1-C_8 alkyl or -C_4-C_8 cycloalkyl, wherein said alkyl or cycloalkyl of R^{10} is optionally substituted with from one to six substituents selected from R^{10a} wherein R^{10a} is selected from halo, -C_1-C_4 alkyl, -C_4-C_8 cycloalkyl, -(5-15 membered) heteroaryl or -C_1-C_4 hydroxyalkyl; or –NR^9R^{10} is a -(4-6 membered) heterocycloalkyl optionally substituted with from one to six substituents selected from halo, -C_1-C_4 alkyl or -C_1-C_4 hydroxyalkyl.

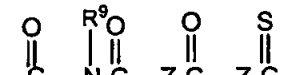
In another aspect of the above embodiment, R^7 is a -C_1-C_8 alkyl substituted by a -C_4-C_8 cycloalkyl; -(C_5-C_{20}) bi- or tricycloalkyl, -(4-8 membered) heterocycloalkyl, -(7-12 membered) heterobi- or heterotricycloalkyl, -C_6-C_{14} aryl, benzo(C_3-C_8 cycloalkyl), -(5-15 membered) heteroaryl, wherein R^7 is optionally independently substituted with from one to six substituents independently selected from R^{7a}, wherein R^{7a} is –NR^9R^{10}, halo, -C_1-C_4 alkyl or -C_1-C_4 hydroxyalkyl.

In another aspect of the above embodiment, R^7 is a -C_1-C_6 alkyl substituted by a -(4-8 membered) heterocycloalkyl or -C_6-C_{14} aryl, wherein R^7 is optionally independently substituted with from one to six substituents independently selected from R^{7a}, wherein R^{7a} is –NR^9R^{10},

halo, -OH, -C_1-C_4 alkyl or -C_1-C_4 hydroxyalkyl, wherein said alkyl or hydroxyalkyl is optional substituted with from one to six halo.

In another aspect of the above embodiment, A is absent and R^1 is benzo(C_5-C_6 cycloalkyl) optionally substituted with from one to three substituents independently selected from -C_1-C_6 alkyl, halo and -OH; or A is ; Z is –CH_2, –CH(OH) or –CH(C_1-C_6 alkyl) and R^1 is -C_1-C_{10} alkyl, -C_6-C_{10} aryl or (6-10 membered) heteroaryl, wherein said alkyl, aryl and heteroaryl are optionally independently substituted with from one to three substituents independently selected from -C_1-C_6 alkyl, halo and -OH; R^2 is H or -C_1-C_6 alkyl; R^3 is H, –$CH_2CH_2SCH_3$, –$CH_2CH_2OCH_3$ or -C_1-C_6 alkyl; R^4 is H and R^6 is H or -C_1-C_6 alkyl.

In an another embodiment, the present invention relates to compounds of Formula I

wherein A is absent or is selected from  ;

Z is selected from –CH_2, –CH(OH), –CH(C_1-C_6 alkyl), –CH(C_1-C_6 alkoxy), -CH(NR^9R^{10}), –CH(CH_2(OH)), –CH(CH(C_1-C_4 alkyl)(OH)) and –CH(C(C_1-C_4 alkyl)(C_1-C_4alkyl)(OH));

R^1 is selected from -C_1-C_{20} alkyl, -C_2-C_{20} alkenyl, -C_2-C_{20} alkynyl, -C_1-C_{20} alkoxy, -C_2-C_{20} alkenoxy, -C_1-C_{20} hydroxyalkyl, -C_3-C_8 cycloalkyl, benzo(C_3-C_8 cycloalkyl), benzo(C_3-C_8 heterocycloalkyl), -C_4-C_8 cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, benzo(C_5-C_{11})bi- or tricycloalkyl, (C_7-C_{11})bi- or tricycloalkenyl, -(3-8 membered) heterocycloalkyl, -C_6-C_{14} aryl and -(5-14 membered) heteroaryl, wherein R^1 is optionally substituted by R^{1a};

wherein R^{1a} in each instance is independently selected from –OH, halo, -C_1-C_6 alkoxy, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

wherein said alkoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{1a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{1b};

wherein R^{1b} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

R^2 is selected from H, -C_1-C_6 alkyl, -C_2-C_6 alkenyl, -C_3-C_8 cycloalkyl and C_3-C_8 cycloalkenyl, wherein R^2 is optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkyl optionally substituted with from one to three halo atoms, -C_1-C_4 alkoxy optionally substituted with from one to three halo atoms, halo and -OH;

or R^1 and R^2 together with the A group when present and the nitrogen atom to which R^2 is attached, or R^1 and R^2 together with the nitrogen atom to which R^1 and R^2 are attached when A is absent, may optionally form a four to eight membered ring;

R^3 is selected from H, -C_1-C_6 alkyl, -C_2-C_6 alkenyl, -C_2-C_8 alkynyl, -C_3-C_8 cycloalkyl, -C_5-C_8 cycloalkenyl and (3-8 membered) heterocycloalkyl -C_6-C_{14} aryl and (5-14 membered) heteroaryl, wherein said alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl aryl or heteroaryl are each optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkoxy, halo, -OH, -S(C_1-C_4)alkyl -C_1-C_4 alkyl -C(=O)OR^9, -SO_2R^9 and -(3-8 membered) heterocycloalkyl wherein said alkyl, alkoxy, and heterocyloalkyl may be further substituted by one to six halo;

R^4 is H, -C_1-C_6 alkyl or halo;

or R^3 and R^4 may together with the carbon atom to which they are attached optionally form a moiety selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, morpholino, piperidino, pyrrolidino, tetrahydrofuranyl and perhydro-2H-pyran, wherein said moiety formed by R^3 and R^4 is optionally substituted with from one to three substituents independently selected from -C_1-C_6 alkyl optionally substituted with from one to three halo atoms, -C_1-C_6 alkoxy optionally substituted with from one to three halo atoms, halo, -OH, -CN and allyl;

R^6 is selected from H, -C_1-C_6 alkyl, -C_2-C_6 alkylene, -C_1-C_6 alkoxy, halo, -CN, -C_3-C_{12} cycloalkyl, -C_4-C_{12} cycloalkenyl -(5-10 membered) heteroaryl and -C_6-C_{10} aryl, wherein said alkyl, alkylene and alkoxy of R^6 are each optionally independently substituted with from one to three substituents independently selected from halo and –CN, and wherein said cycloalkyl, cycloalkenyl, heteroaryl and aryl of R^6 are each optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkyl optionally substituted with from one to three halo atoms, -C_1-C_4 alkoxy optionally substituted with from one to three halo atoms, halo and –CN;

R^7 is selected from -C_1-C_{20} alkyl, -C_1-C_{20} alkoxy, -C_1-C_{20} hydroxyalkyl, -C_3-C_{12} cycloalkyl, -C_4-C_{12} cycloalkenyl, -(C_5-C_{20}) bi- or tricycloalkyl, -(C_7-C_{20})bi- or tricycloalkenyl, (3-12 membered) heterocycloalkyl, -(7-20 membered) heterobi- or heterotricycloalkyl, -C_6-C_{14} aryl, -(5-15 membered) heteroaryl -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy, wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenoxy, alkynoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^7 are each independently substituted with from one to six substituents independently

selected from the group R^{7a} or are each independently optionally substituted with from one to six substituents independently selected from the group R^{7d}

wherein R^{7a} in each instance is independently selected from -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -C_3-C_{15} cycloalkyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy, wherein said alkyl, alkoxy, alkoxyalkyl, cycloalkyl, heterocycloalkyl, aryl heteroaryl, aryloxy, and heteroaryloxy of R^{7a} are each independently substituted by R^{7b} ;

wherein R^{7d} in each instance is independently selected from: -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -SO_2-NR^9R^{10}, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, ;wherein said alkenyl, alkynyl, hydroxyalkyl, alkenoxy, alkynoxy, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, of $R^{7d}$are each optionally independently substituted with from one to six substituents independently selected from the group R^{7b};

wherein R^{7b} in each instance is independently selected from -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

or R^6 and R^7 may together with the carbon and nitrogen atoms to which they are respectively attached optionally form a (5-8 membered) heterocycloalkyl ring, a (5-8 membered) heterocycloalkenyl ring or a (6-8 membered) heteroaryl ring, wherein said heterocycloalkyl, heterocycloalkenyl and heteroaryl rings are each optionally independently substituted with from one to three substituents independently selected from halo, -C_1-C_6 alkyl, optionally subsituted with from one to three halo atoms, -C_1-C_6 alkoxy optionally subsituted with from one to three halo atoms, -C_1-C_6 hydroxyalkyl, -OH, -$(CH_2)_{zero\text{-}10}NR^9R^{10}$, -$(CH_2)_{zero\text{-}10}C(=O)NR^9R^{10}$, -$SO_2NR^9R^{10}$ and -C_3-C_{12} cycloalkyl;

R^9 and R^{10} in each instance are each independently selected from -H, -$C(=O)R^{13}$ or -C_1-C_{20} alkyl, wherein at least one of R^9 and R^{10} are -$C(=O)R^{13}$ or -C_1-C_{20} alkyl, and wherein each -C_1-C_{20} alkyl is substituted with R^{10a}

wherein R^{10a} in each instance is independently selected from -C_1-C_6 alkoxy, -CN, -NO_2, -$NR^{11}R^{11}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy; wherein said alkoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy

of R^{10a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{10b}

wherein R^{10b} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_nR^{11}$, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy

or NR^9R^{10} may form a (4-20 membered) heterocycloalkyl, (5-18 membered) heterobi- or tricycloalkyl, (5-18 membered) heterobi- or tricycloalkenyl, or -(5-15 membered) heteroaryl, wherein said heterocycloalkyl, heterobi- or tricycloalkyl, heterobi- or tricycloalkenyl or heteroaryl are optionally independently substituted with from one to six substituents independently selected from -C_1-C_6 alkyl, -C_2-C_6 alkenyl, -C_2-C_6 alkenyl, -C_1-C_6 alkoxy, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, -C_1-C_6 hydroxyalkyl, -C_2-C_6 hydroxyalkenyl, -C_2-C_6 hydroxyalkenyl, halo, -OH, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -$S(O)_nR^{11}$ and -$S(O)_nNR^{11}R^{12}$;

R^{11} and R^{12} in each instance are each independently selected from H, -C_1-C_8 alkyl, -C_3-C_8 cycloalkyl, -C_4-C_8 cycloalkenyl, (C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, (3-8 membered) heterocycloalkyl, -C_6-C_{10} aryl and (5-14 membered) heteroaryl, wherein said alkyl of R^{11} and $R^{12}$is optionally independently substituted with from one to three substituents independently selected from –OH, -CN and -C_3-C_8 cycloalkyl, and wherein each hydrogen atom of said alkyl is optionally independently replaced with a halo atom, and wherein said cycloalkyl, cycloalkenyl, heterocycloalkyl, aryl and hetereoaryl of R^{11} and R^{12} are each optionally independently substituted with from one to three substituents independently selected from halo, -C_1-C_8 alkyl optionally substituted with from one to three halo atoms, -OH, -CN and -C_3-C_8 cycloalkyl;

R^{13} is in each instance is independently selected from alkyl substituted by -C_1-C_{12} alkoxy, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy; wherein said alkoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{13} is optionally substituted by one to three substituents independently selected from halo, -C_1-C_8 alkyl optionally substituted with from one to three halo atoms, -OH, -CN and -C_3-C_8 cycloalkyl;

n is in each instance an integer independently selected from zero, 1 and 2;

or a pharmaceutically acceptable salt thereof.

In one aspect of the above embodiment, R^7 is a -C_1-C_8 alkyl substituted by R^{7a}; R^{7a} is $-NR^9R^{10}$; R^9 is H or methyl; R^{10} is a -C_1-C_8 alkyl; R^{10a} is -C_1-C_6 alkoxy, $-C_4$-C_8 cycloalkyl, -(4-8 membered) heterocycloalkyl, -C_6-C_{15} aryl or -(5-15 membered) heteroaryl, wherein said alkoxy, cycloalkyl, heterocycloalkyl, aryl, heteroaryl of R^{10a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{10b}; wherein R^{10b} is halo, -OH, -C_1-C_4 alkyl or -C_1-C_4 hydroxyalkyl, wherein said alkyl or hydroxyalkyl of R^{10b} is optionally substituted by one to six halo.

In another aspect of the above embodiment, R^7 is a -C_1-C_8 alkyl substituted by R^{7a}; R^{7a} is $-C(=O)NR^9R^{10}$; R^9 is H or methyl; R^{10} is a -C_1-C_8 alkyl; R^{10a} is -C_1-C_6 alkoxy, $-C_4$-C_8 cycloalkyl, -(4-8 membered) heterocycloalkyl, -C_6-C_{15} aryl or -(5-15 membered) heteroaryl, wherein said alkoxy, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{10a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{10b}; wherein R^{10b} is halo, -OH, -C_1-C_4 alkyl or -C_1-C_4 hydroxyalkyl, wherein said alkyl or hydroxyalkyl of R^{10b} is optionally substituted by one to six halo.

In another aspect of the above embodiment A is absent and R^1 is benzo(C_5-C_8 cycloalkyl) optionally substituted with from one to three substituents independently selected from C_1-C_6 alkyl, halo and OH; or A is $-Z-\overset{O}{\overset{\|}{C}}-$; Z is $-CH_2$, –CH(OH) or –CH(C_1-C_6 alkyl) and R^1 is C_1-C_{10} alkyl, C_6-C_{10} aryl or (6-10 membered) heteroaryl, wherein said alkyl, aryl and heteroaryl are optionally independently substituted with from one to three substituents independently selected from C_1-C_6 alkyl, halo and OH; R^2 is H or C_1-C_6 alkyl; R^3 is H, $-CH_2CH_2SCH_3$, $-CH_2CH_2OCH_3$ or C_1-C_6 alkyl; R^4 is H and R^6 is H or C_1-C_6 alkyl.

In an another embodiment, the present invention relates to compounds of Formula I

wherein A is absent or is selected from $\overset{O}{\overset{\|}{C}}$- , -N($R^9$)$\overset{O}{\overset{\|}{C}}$-, -Z-$\overset{O}{\overset{\|}{C}}$-, -Z-$\overset{S}{\overset{\|}{C}}$- and SO_2;

Z is selected from $-CH_2$, –CH(OH), –CH(C_1-C_6 alkyl), –CH(C_1-C_6 alkoxy), -CH(NR^9R^{10}), –CH(CH_2(OH)), –CH(CH(C_1-C_4 alkyl)(OH)) and –CH(C(C_1-C_4 alkyl)(C_1-C_4alkyl)(OH));

R^1 is selected from -C_1-C_{20} alkyl, -C_2-C_{20} alkenyl, -C_2-C_{20} alkynyl, -C_1-C_{20} alkoxy, -C_2-C_{20} alkenoxy, -C_1-C_{20} hydroxyalkyl, -C_3-C_8 cycloalkyl, benzo(C_3-C_8 cycloalkyl), benzo(C_3-C_8 heterocycloalkyl), -C_4-C_8 cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, benzo(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(3-8 membered) heterocycloalkyl, -C_6-C_{14} aryl and -(5-14 membered) heteroaryl,wherein R1 is optionally substituted by R^{1a};

wherein R^{1a} in each instance is independently selected from –OH, halo, -C_1-C_6 alkoxy, -CN, -NO_2, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-NR^9R^{10}, -$S(O)_n$-

R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy,

wherein said alkoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{1a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{1b};

wherein R^{1b} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

R^2 is selected from H, -C_1-C_8 alkyl, -C_2-C_6 alkenyl, -C_3-C_8 cycloalkyl and -C_3-C_8 cycloalkenyl, wherein R^2 is optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkyl optionally substituted with from one to three halo atoms, -C_1-C_4 alkoxy optionally substituted with from one to three halo atoms, halo and -OH;

or R^1 and R^2 together with the A group when present and the nitrogen atom to which R^2 is attached, or R^1 and R^2 together with the nitrogen atom to which R^1 and R^2 are attached when A is absent, may optionally form a four to eight membered ring;

R^3 is selected from -C_6-C_{14} aryl and (5-14 membered) heteroaryl, wherein said aryl or heteroaryl are each optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkoxy, halo, -OH, -S(C_1-C_4)alkyl -C_1-C_4 alkyl -C(=O)OR^9, -SO_2R^9 and (3-8 membered) heterocycloalkyl wherein said alkyl, alkoxy, and heterocyloalkyl may be further substituted by one to six halo;

R^4 is H, -C_1-C_6 alkyl or halo;

or R^3 and R^4 may together with the carbon atom to which they are attached optionally form a moiety selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, morpholino, piperidino, pyrrolidino, tetrahydrofuranyl and perhydro-2H-pyran, wherein said moiety formed by R^3 and R^4 is optionally substituted with from one to three substituents independently selected from -C_1-C_6 alkyl optionally substituted with from one to three halo atoms, -C_1-C_6 alkoxy optionally substituted with from one to three halo atoms, halo, -OH, -CN and allyl;

R^6 is selected from H, -C_1-C_6 alkyl, -C_2-C_6 alkylene, -C_1-C_8 alkoxy, halo, -CN, -C_3-C_{12} cycloalkyl, -C_4-C_{12} cycloalkenyl (5-10 membered) heteroaryl and -C_6-C_{10} aryl, wherein said alkyl, alkylene and alkoxy of R^6 are each optionally independently substituted with from one to three substituents independently selected from halo and –CN, and wherein said cycloalkyl,

cycloalkenyl, heteroaryl and aryl of R^6 are each optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkyl optionally substituted with from one to three halo atoms, -C_1-C_4 alkoxy optionally substituted with from one to three halo atoms, halo and –CN;

R^7 is selected from H, -C_1-C_{20} alkyl, -C_1-C_{20} alkoxy, -C_1-C_{20} hydroxyalkyl, -C_3-C_{12} cycloalkyl, -C_4-C_{12} cycloalkenyl, (C_5-C_{20}) bi- or tricycloalkyl, -(C_7-C_{20})bi- or tricycloalkenyl, (3-12 membered) heterocycloalkyl, -(7-20 membered) heterobi- or heterotricycloalkyl, -C_6-C_{14} aryl and -(5-15 membered) heteroaryl, wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenoxy, alkynoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^7 are each optionally independently substituted with from one to six substituents independently selected from the group R^{7a};

wherein R^{7a} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl, -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy; wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenoxy, alkynoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{7a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{7b};

wherein R^{7b} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{11}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

or R^6 and R^7 may together with the carbon and nitrogen atoms to which they are respectively attached optionally form a (5-8 membered) heterocycloalkyl ring, a (5-8 membered) heterocycloalkenyl ring or a (6-8 membered) heteroaryl ring, wherein said heterocycloalkyl, heterocycloalkenyl and heteroaryl rings are each optionally independently substituted with from one to three substituents independently selected from halo, -C_1-C_6 alkyl, optionally subsituted with from one to three halo atoms, -C_1-C_6 alkoxy optionally subsituted with from one to three halo atoms, -C_1-C_6 hydroxyalkyl, -OH, -$(CH_2)_{zero\text{-}10}NR^9R^{10}$, -$(CH_2)_{zero\text{-}10}$C(=O)$NR^9R^{10}$, -$SO_2NR^9R^{10}$ and -C_3-C_{12} cycloalkyl;

R^9 and R^{10} in each instance are each independently selected from H, -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl,

-C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-$NR^{10}R^{11}$, -$S(O)_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy, wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenoxy, alkynoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^9 of R^{10} are each optionally independently substituted with from one to six substituents independently selected from the group R^{10a};

wherein R^{10a} in each instance is independently selected from –OH, halo, -C_1-C_6 alkoxy, -CN, -NO_2, -$NR^{11}R^{12}$, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy; wherein said alkoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{10a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{10b};

wherein R^{10b} in each instance is independently selected from -OH, halo; -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -$NR^{11}R^{12}$, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

or NR^9R^{10} may form may form a -(4-20 membered) heterocycloalkyl, -(5-18 membered) heterobi- or tricycloalkyl, -(5-18 membered) heterobi- or tricycloalkenyl, or -(5-15 membered) heteroaryl, wherein said heterocycloalkyl, heterobi- or tricycloalkyl, heterobi- or tricycloalkenyl or heteroaryl are optionally independently substituted with from one to six substituents independently selected from -C_1-C_6 alkyl, -C_2-C_6 alkenyl, -C_2-C_6 alkenyl, -C_1-C_6 alkoxy, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, -C_1-C_6 hydroxyalkyl, -C_2-C_6 hydroxyalkenyl, -C_2-C_6 hydroxyalkenyl, halo, -OH, -CN, -NO_2, -$NR^{11}R^{12}$, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{11}, -$S(O)_nR^{11}$ and -$S(O)_nNR^{11}R^{12}$;

wherein R^{11} and R^{12} in each instance are each independently selected from H, -C_1-C_8 alkyl, -C_3-C_8 cycloalkyl, -C_4-C_8 cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(3-8 membered) heterocycloalkyl, -C_6-C_{10} aryl and -(5-14 membered) heteroaryl, wherein said alkyl of R^{11} is optionally independently substituted with from one to three substituents independently selected from –OH, -CN and -C_3-C_8 cycloalkyl, and wherein each hydrogen atom of said alkyl is optionally independently replaced with a halo atom, and wherein said cylcoalkyl, cycloalkenyl, heterocycloalkyl, aryl and hetereoaryl of R^{11} are each

optionally independently substituted with from one to three substituents independently selected from halo, -C_1-C_8 alkyl optionally substituted with from one to three halo atoms, -OH, -CN and -C_3-C_8 cycloalkyl; and

n is in each instance an integer independently selected from zero, 1 and 2;

or a pharmaceutically acceptable salt thereof.

In an another embodiment, the present invention relates to compounds of Formula I, wherein A is absent;

R^1 is -C_1-C_{20} alkyl; wherein R^1 is independently substituted with from one to six substituents independently selected from R^{1A};

wherein R^{1a} in each instance is independently selected from -C_1-C_8 alkoxy, -CN, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

wherein said cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{1a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{1b};

wherein R^{1b} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_8 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_8 alkenoxy, -C_2-C_8 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

R^2 is selected from H, -C_1-C_8 alkyl, -C_2-C_8 alkenyl, -C_3-C_8 cycloalkyl and -C_3-C_8 cycloalkenyl, wherein R^2 is optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkyl optionally substituted with from one to three halo atoms, -C_1-C_4 alkoxy optionally substituted with from one to three halo atoms, halo and -OH;

R^3 is selected from H, -C_1-C_8 alkyl, -C_2-C_8 alkenyl, -C_2-C_8 alkynyl, -C_3-C_8 cycloalkyl, -C_5-C_8 cycloalkenyl and (3-8 membered) heterocycloalkyl, -C_6-C_{14} aryl and (5-14 membered) heteroaryl, wherein said alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl aryl or heteroaryl are each optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkoxy, halo, -OH, -S(C_1-C_4)alkyl -C_1-C_4alkyl -$C(=O)OR^9$, -SO_2R^9 and (3-8 membered) heterocycloalkyl wherein said alkyl, alkoxy, and heterocyloalkyl may be further substituted by one to six halo;

R^4 is H, -C_1-C_8 alkyl or halo;

or R^3 and R^4 may together with the carbon atom to which they are attached optionally form a moiety selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, morpholino, piperidino, pyrrolidino, tetrahydrofuranyl and perhydro-2H-pyran, wherein said moiety formed by R^3 and R^4 is optionally substituted with from one to three substituents independently selected from -C_1-C_8 alkyl optionally substituted with from one to three halo atoms, -C_1-C_8 alkoxy optionally substituted with from one to three halo atoms, halo, -OH, -CN and allyl;

R^6 is selected from H, -C_1-C_6 alkyl, -C_2-C_6 alkylene, -C_1-C_6 alkoxy, halo, -CN, -C_3-C_{12} cycloalkyl, -C_4-C_{12} cycloalkenyl (5-10 membered) heteroaryl and -C_6-C_{10} aryl, wherein said alkyl, alkylene and alkoxy of R^6 are each optionally independently substituted with from one to three substituents independently selected from halo and –CN, and wherein said cycloalkyl, cycloalkenyl, heteroaryl and aryl of R^6 are each optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkyl optionally substituted with from one to three halo atoms, -C_1-C_4 alkoxy optionally substituted with from one to three halo atoms, halo and –CN;

R^7 is selected from H, -C_1-C_{20} alkyl, -C_1-C_{20} alkoxy, -C_1-C_{20} hydroxyalkyl, -C_3-C_{12} cycloalkyl, -C_4-C_{12} cycloalkenyl, -(C_5-C_{20}) bi- or tricycloalkyl, -(C_7-C_{20})bi- or tricycloalkenyl, (3-12 membered) heterocycloalkyl, (-7-20 membered) heterobi- or heterotricycloalkyl, -C_6-C_{14} aryl and (5-15 membered) heteroaryl, wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenoxy, alkynoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^7 are each optionally independently substituted with from one to six substituents independently selected from the group R^{7a};

wherein R^{7a} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl, -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{16} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy; wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenoxy, alkynoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{7a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{7b};

wherein R^{7b} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{11}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

or R^6 and R^7 may together with the carbon and nitrogen atoms to which they are respectively attached optionally form a -(5-8 membered) heterocycloalkyl ring, a -(5-8 membered) heterocycloalkenyl ring or a -(6-8 membered) heteroaryl ring, wherein said heterocycloalkyl, heterocycloalkenyl and heteroaryl rings are each optionally independently substituted with from one to three substituents independently selected from halo, $-C_1$-C_6 alkyl, optionally subsituted with from one to three halo atoms, $-C_1$-C_6 alkoxy optionally subsituted with from one to three halo atoms, $-C_1$-C_6 hydroxyalkyl, -OH, $-(CH_2)_{zero\text{-}10}NR^9R^{10}$, $-(CH_2)_{zero\text{-}10}C(=O)NR^9R^{10}$, $-SO_2NR^9R^{10}$ and $-C_3$-C_{12} cycloalkyl;

R^9 and R^{10} in each instance are each independently selected from H, -OH, $-C_1$-C_{12} alkyl, $-C_2$-C_{12} alkenyl, $-C_2$-C_{12} alkynyl, $-C_1$-C_6 alkoxy, $-C_1$-C_{12} alkoxyalkyl $-C_1$-C_{12} hydroxyalkyl, $-C_2$-C_8 alkenoxy, $-C_2$-C_6 alkynoxy, $-C(=O)NR^{11}R^{12}$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-SO_2$-$NR^{11}R^{12}$, $-S(O)_n$-R^{11}, $-C_3$-C_{15} cycloalkyl, $-C_4$-C_{15} cycloalkenyl, $-(C_5$-$C_{11})$bi- or tricycloalkyl, $-(C_7$-$C_{11})$bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, $-C_6$-C_{15} aryl, -(5-15 membered) heteroaryl, $-C_6$-C_{15} aryloxy and -(5-15 membered) heteroaryloxy, wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenoxy, alkynoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^9 of R^{10} are each optionally independently substituted with from one to six substituents independently selected from the group R^{10a};

wherein R^{10a} in each instance is independently selected from –OH, Halo, $-C_1$-C_6 alkoxy, -CN, $-NO_2$, $-NR^{11}R^{12}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)R^{11}$, $-C(=O)OR^{12}$, $-SO_2$-$NR^{11}R^{12}$, $-S(O)_n$-R^{11}, $-C_3$-C_{15} cycloalkyl, $-C_4$-C_{15} cycloalkenyl, $-(C_5$-$C_{11})$bi- or tricycloalkyl, $-(C_7$-$C_{11})$bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, $-C_6$-C_{15} aryl, -(5-15 membered) heteroaryl, $-C_6$-C_{15} aryloxy and -(5-15 membered) heteroaryloxy; wherein said alkoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{10a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{10b};

wherein R^{10b} in each instance is independently selected from -OH, halo; $-C_1$-C_{12} alkyl, $-C_2$-C_{12} alkenyl, $-C_2$-C_{12} alkynyl, $-C_1$-C_6 alkoxy, $-C_1$-C_{12} alkoxyalkyl $-C_1$-C_{12} hydroxyalkyl, $-C_2$-C_6 alkenoxy, $-C_2$-C_6 alkynoxy, halo, -CN, $-NO_2$, $-NR^{11}R^{12}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-SO_2$-$NR^{11}R^{12}$, $-S(O)_n$-R^{11}, $-C_3$-C_{15} cycloalkyl, $-C_4$-C_{15} cycloalkenyl, $-(C_5$-$C_{11})$bi- or tricycloalkyl, $-(C_7$-$C_{11})$bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, $-C_6$-C_{15} aryl, -(5-15 membered) heteroaryl, $-C_6$-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

or NR^9R^{10} may form a (4-20 membered) heterocycloalkyl, (5-18 membered) heterobi- or tricycloalkyl (5-18 membered) heterobi- or tricycloalkenyl, or -(5-15 membered) heteroaryl, wherein said a heterocycloalkyl, heterobi- or tricycloalkyl, heterobi- or tricycloalkenyl or heteroaryl are optionally independently substituted with from one to six substituents independently selected from $-C_1$-C_6 alkyl, $-C_2$-C_6 alkenyl, $-C_2$-C_6 alkenyl, $-C_1$-C_6 alkoxy, $-C_2$-C_6

alkenoxy, -C_2-C_6 alkynoxy,-C_1-C_6 hydroxyalkyl,-C_2-C_6 hydroxyalkenyl,-C_2-C_6 hydroxyalkenyl, halo, -OH, -CN, -NO_2, -$NR^{11}R^{12}$, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{11}, -S(O)$_n$$R^{11}$ and -S(O)$_n$$NR^{11}R^{12}$;

R^{11} and R^{12} in each instance are each independently selected from H, -C_1-C_8 alkyl, -C_3-C_8 cycloalkyl,-C_4-C_8 cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(3-8 membered) heterocycloalkyl, -C_6-C_{10} aryl and -(5-14 membered) heteroaryl, wherein said alkyl of R^{11} is optionally independently substituted with from one to three substituents independently selected from –OH, -CN and-C_3-C_8 cycloalkyl, and wherein each hydrogen atom of said alkyl is optionally independently replaced with a halo atom, and wherein said cycloalkyl, cycloalkenyl, heterocycloalkyl, aryl and hetereoaryl of R^{11} are each optionally independently substituted with from one to three substituents independently selected from halo,-C_1-C_8 alkyl optionally substituted with from one to three halo atoms, -OH, -CN and-C_3-C_8 cycloalkyl; and

n is in each instance an integer independently selected from zero, 1 and 2;

or a pharmaceutically acceptable salt thereof.

Compounds of Formula I may have optical centers and therefore may occur in different enantiomeric and diastereomeric configurations. The present invention includes all enantiomers, diastereomers, and other stereoisomers of such compounds of Formula I, as well as racemic compounds and racemic mixtures and other mixtures of stereoisomers thereof.

Pharmaceutically acceptable salts of the compounds of Formula I include the acid addition and base salts thereof.

Suitable acid addition salts are formed from acids which form non-toxic salts. Examples include, but are not limited to, the acetate, adipate, aspartate, benzoate, besylate, bicarbonate/carbonate, bisulphate/sulphate, borate, camsylate, citrate, cyclamate, edisylate, esylate, formate, fumarate, gluceptate, gluconate, glucuronate, hexafluorophosphate, hibenzate, hydrochloride/chloride, hydrobromide/bromide, hydroiodide/iodide, isethionate, lactate, malate, maleate, malonate, mandelates mesylate, methylsulphate, naphthylate, 2-napsylate, nicotinate, nitrate, orotate, oxalate, palmitate, pamoate, phosphate/hydrogen phosphate/dihydrogen phosphate, pyroglutamate, salicylate, saccharate, stearate, succinate, sulfonate, stannate, tartrate, tosylate, trifluoroacetate and xinofoate salts.

Suitable base salts are formed from bases which form non-toxic salts. Examples include, but are not limited to, the aluminium, arginine, benzathine, calcium, choline, diethylamine, diolamine, glycine, lysine, magnesium, meglumine, olamine, potassium, sodium, tromethamine and zinc salts.

Hemisalts of acids and bases may also be formed, for example, hemisulphate and hemicalcium salts.

For a review on suitable salts, see Handbook of Pharmaceutical Salts: Properties, Selection, and Use by Stahl and Wermuth (Wiley-VCH, 2002).

Pharmaceutically acceptable salts of compounds of Formula I may be prepared by one or more of three methods:

(i) by reacting the compound of Formula I with the desired acid or base;

(ii) by removing an acid- or base-labile protecting group from a suitable precursor of the compound of Formula I or by ring-opening a suitable cyclic precursor, for example, a lactone or lactam, using the desired acid or base; or

(iii) by converting one salt of the compound of Formula I to another by reaction with an appropriate acid or base or by means of a suitable ion exchange column.

All three reactions are typically carried out in solution. The resulting salt may precipitate out and be collected by filtration or may be recovered by evaporation of the solvent. The degree of ionization in the resulting salt may vary from completely ionised to almost non-ionised.

The compounds of the invention may exist in a continuum of solid states ranging from fully amorphous to fully crystalline. The term 'amorphous' refers to a state in which the material lacks long range order at the molecular level and, depending upon temperature, may exhibit the physical properties of a solid or a liquid. Typically such materials do not give distinctive X-ray diffraction patterns and, while exhibiting the properties of a solid, are more formally described as a liquid. Upon heating, a change from solid to liquid properties occurs which is characterised by a change of state, typically second order ('glass transition'). The term 'crystalline' refers to a solid phase in which the material has a regular ordered internal structure at the molecular level and gives a distinctive X-ray diffraction pattern with defined peaks. Such materials when heated sufficiently will also exhibit the properties of a liquid, but the change from solid to liquid is characterised by a phase change, typically first order ('melting point').

The compounds of the invention may also exist in unsolvated and solvated forms. The term 'solvate' is used herein to describe a molecular complex comprising the compound of the invention and one or more pharmaceutically acceptable solvent molecules, for example, ethanol. The term 'hydrate' is employed when said solvent is water.

A currently accepted classification system for organic hydrates is one that defines isolated site, channel, or metal-ion coordinated hydrates - see Polymorphism in Pharmaceutical Solids by K. R. Morris (Ed. H. G. Brittain, Marcel Dekker, 1995). Isolated site hydrates are ones in which the water molecules are isolated from direct contact with each other by intervening organic molecules. In channel hydrates, the water molecules lie in lattice channels where they are next to other water molecules. In metal-ion coordinated hydrates, the water molecules are bonded to the metal ion.

When the solvent or water is tightly bound, the complex will have a well-defined stoichiometry independent of humidity. When, however, the solvent or water is weakly bound, as in channel solvates and hygroscopic compounds, the water/solvent content will be dependent on humidity and drying conditions. In such cases, non-stoichiometry will be the norm.

The compounds of the invention may also exist in a mesomorphic state (mesophase or liquid crystal) when subjected to suitable conditions. The mesomorphic state is intermediate between the true crystalline state and the true liquid state (either melt or solution). Mesomorphism arising as the result of a change in temperature is described as 'thermotropic' and that resulting from the addition of a second component, such as water or another solvent, is described as 'lyotropic'. Compounds that have the potential to form lyotropic mesophases are described as 'amphiphilic' and consist of molecules which possess an ionic (such as $-COO^-Na^+$, $-COO^-K^+$, or $-SO_3^-Na^+$) or non-ionic (such as $-N^+N^+(CH_3)_3$) polar head group. For more information, see Crystals and the Polarizing Microscope by N. H. Hartshorne and A. Stuart, 4th Edition (Edward Arnold, 1970).

Hereinafter all references to compounds of Formula I include references to salts, solvates, multi-component complexes and liquid crystals thereof and to solvates, multi-component complexes and liquid crystals of salts thereof.

The compounds of the invention include compounds of Formula I as hereinbefore defined, including all polymorphs and crystal habits thereof, prodrugs and isomers thereof (including optical, geometric and tautomeric isomers) as hereinafter defined and isotopically-labeled compounds of Formula I.

Unless otherwise indicated, as used herein, the term "A is absent" means a direct bond between the nitrogen and R^1 (i.e., $-N-R^1$).

Unless otherwise indicated, as used herein, the terms "halogen" and "halo" include F, Cl, Br, and I.

Unless otherwise indicated, as used herein, the term "alkyl" includes saturated monovalent hydrocarbon radicals having straight or branched moieties. Examples of alkyl groups include, but are not limited to, methyl, ethyl, *n*-propyl, isopropyl, and *t*-butyl.

Unless otherwise indicated, as used herein, the term "alkenyl" includes alkyl moieties having at least one carbon-carbon double bond wherein alkyl is as defined above. Examples of alkenyl include, but are not limited to, ethenyl and propenyl.

Unless otherwise indicated, as used herein, the term "alkynyl" includes alkyl moieties having at least one carbon-carbon triple bond wherein alkyl is as defined above. Examples of alkynyl groups include, but are not limited to, ethynyl and 2-propynyl.

Unless otherwise indicated, as used herein, the term "alkoxy", means "alkyl-O-", wherein "alkyl" is as defined above. Examples of "alkoxy" groups include, but are not limited to, methoxy, ethoxy, propoxy, butoxy, pentoxy and allyloxy.

Unless otherwise indicated, as used herein, the term "alkenoxy", means "alkenyl-O-", wherein "alkenyl" is as defined above.

Unless otherwise indicated, as used herein, the term "cycloalkyl" includes non-aromatic saturated cyclic alkyl moieties wherein alkyl is as defined above. Examples of cycloalkyl include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl. "Bicycloalkyl" and "tricycloalkyl" groups are non-aromatic saturated carbocyclic groups consisting of two or three rings respectively, wherein said rings share at least one carbon atom. Unless otherwise indicated, for purposes of the present invention, bicycloalkyl groups include spiro groups and fused ring groups. Examples of bicycloalkyl groups include, but are not limited to, bicyclo-[3.1.0]-hexyl, bicyclo—2.2.1]-hept-1-yl, norbornyl, spiro[4.5]decyl, spiro[4.4]nonyl, spiro[4.3]octyl, and spiro[4.2]heptyl. An example of a tricycloalkyl group is adamantanyl. Other cycloalkyl, bicycloalkyl, and tricycloalkyl groups are known in the art, and such groups are encompassed by the definitions "cycloalkyl", "bicycloalkyl" and "tricycloalkyl" herein.

"Cycloalkenyl", "bicycloalkenyl", and "tricycloalkenyl" refer to non-aromatic carbocyclic cycloalkyl, bicycloalkyl, and tricycloalkyl moieties as defined above, except comprising one or more carbon-carbon double bonds connecting carbon ring members (an "endocyclic" double bond) and/or one or more carbon-carbon double bonds connecting a carbon ring member and an adjacent non-ring carbon (an "exocyclic" double bond). Examples of cycloalkenyl groups include, but are not limited to, cyclopentenyl, cyclobutenyl, and cyclohexenyl, and a non-limiting example of a bicycloalkenyl group is norbornenyl. Other cycloalkenyl, bicycloalkenyl, and tricycloalkenyl groups are known in the art, and such groups are included within the definitions "cycloalkenyl", "bicycloalkenyl" and "tricycloalkenyl" herein.

Cycloalkyl, cycloalkenyl, bicycloalkyl, and bicycloalkenyl groups also include groups that are substituted with one or more oxo moieties. Examples of such groups with oxo moieties are oxocyclopentyl, oxocyclobutyl, oxocyclopentenyl, and norcamphoryl.

As used herein, the term "benzocycloalkyl" includes, without limitation, moieties such as tetrahydronaphthyl, indanyl, 1,2-benzocylcoheptanyl and the like.

Unless otherwise indicated, as used herein, the term "aryl" includes an organic radical derived from an aromatic hydrocarbon by removal of one hydrogen, such as phenyl, naphthyl, indenyl, indanyl, and fluorenyl. "Aryl" encompasses fused ring groups wherein at least one ring is aromatic.

Unless otherwise indicated, as used herein, the terms "heterocyclic" and "heterocycloalkyl" refer to non-aromatic cyclic groups containing one or more heteroatoms,

prefereably from one to four heteroatoms, each selected from O, S and N. "Heterobicycloalkyl" groups are non-aromatic two-ringed cyclic groups, wherein said rings share one or two atoms, and wherein at least one of the rings contains a heteroatom (O, S, or N). Heterobicycloalkyl groups for purposes of the present invention, and unless otherwise indicated, include spiro groups and fused ring groups. "Heterotricycloalkyl" groups are non-aromatic three-ringed cyclic groups, wherein said rings are fused to one another or form a spiro group (in other words, at least two of said rings share one or two atoms and the third ring shares one or two atoms with at least one of said two rings). The heterotricycloalkyl groups of the compounds of the present invention can include one or more O, S and/or N heteroatoms. In one embodiment, each ring in the heterobicycloalkyl or heterotricycloalkyl contains up to four heteroatoms (i.e. from zero to four heteroatoms, provided that at least one ring contains at least one heteroatom). The heterocycloalkyl, heterobicycloalky and heterotricycloalkyl groups of the present invention can also include ring systems substituted with one or more oxo moieties. The heterocyclic groups, including the heterobicyclic and heterotricyclic groups, may comprise double or triple bonds, e.g. heterocycloalkenyl, heterobicycloalkenyl, and heterotricycloalkenyl. Examples of non-aromatic heterocyclic groups are aziridinyl, azetidinyl, pyrrolidinyl, piperidinyl, azepinyl, piperazinyl, 1,2,3,6-tetrahydropyridinyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydrothienyl, tetrahydropyranyl, tetrahydrothiopyranyl, morpholino, thiomorpholino, thioxanyl, pyrrolinyl, indolinyl, 2H-pyranyl, 4H-pyranyl, dioxanyl, 1,3-dioxolanyl, pyrazolinyl, dihydropyranyl, dihydrothienyl, dihydrofuranyl, pyrazolidinyl, imidazolinyl, imidazolidinyl, 3-azabicyclo[3.1.0]hexanyl, 3-azabicyclo[4.1.0]heptanyl, quinolizinyl, quinuclidinyl, 1,4-dioxaspiro[4.5]decyl, 1,4-dioxaspiro[4.4]nonyl, 1,4-dioxaspiro[4.3]octyl, and 1,4-dioxaspiro[4.2]heptyl.

Unless otherwise indicated, as used herein, "heteroaryl" refers to aromatic groups containing one or more heteroatoms (O, S, or N), preferably from one to four heteroatoms. A multicyclic group containing one or more heteroatoms wherein at least one ring of the group is aromatic is a "heteroaryl" group. The heteroaryl groups of this invention can also include ring systems substituted with one or more oxo moieties. Examples of heteroaryl groups are pyridinyl, pyridazinyl, imidazolyl, pyrimidinyl, pyrazolyl, triazolyl, pyrazinyl, quinolyl, isoquinolyl, 1,2,3,4-tetrahydroquinolyl, tetrazolyl, furyl, thienyl, isoxazolyl, thiazolyl, oxazolyl, isothiazolyl, pyrrolyl, indolyl, benzimidazolyl, benzofuranyl, cinnolinyl, indazolyl, indolizinyl, phthalazinyl, triazinyl, 1,2,4-trizainyl, 1,3,5-triazinyl, isoindolyl, 1-oxoisoindolyl, purinyl, oxadiazolyl, thiadiazolyl, furazanyl, benzofurazanyl, benzothiophenyl, benzotriazolyl, benzothiazolyl, benzoxazolyl, quinazolinyl, quinoxalinyl, naphthyridinyl, dihydroquinolyl, tetrahydroquinolyl, dihydroisoquinolyl, tetrahydroisoquinolyl, benzofuryl, furopyridinyl, pyrolopyrimidinyl, and azaindolyl.

Unless otherwise indicated to the contrary, all the foregoing groups derived from hydrocarbons may be optionally substituted by one or more halogen atoms (e.g., $-CH_2F$, $-CHF_2$ $-CF_3$, -PhCl, etc.).

Unless otherwise indicated, the term "one or more substituents", as used herein, refers to from one to the maximum number of substituents possible based on the number of available bonding sites.

Unless otherwise indicated, all the foregoing groups derived from hydrocarbons may have up to about 1 to about 20 carbon atoms (e.g. C_1-C_{20} alkyl, C_2-C_{20} alkenyl, C_3-C_{20} cycloalkyl, 3-20 membered heterocycloalkyl; C_6-C_{20} aryl, 5-20 membered heteroaryl, etc.) or 1 to about 15 carbon atoms (e.g., C_1-C_{15} alkyl, C_2-C_{15} alkenyl, C_3-C_{15} cycloalkyl, 3-15 membered heterocycloalkyl, C_6-C_{15} aryl, 5-15 membered heteroaryl, etc.) , or 1 to about 12 carbon atoms, or 1 to about 8 carbon atoms, or 1 to about 6 carbon atoms.

As appreciated by the artisan, the use of Formula I is a convenience, and the invention is understood to envision and embrace each and every species thereunder as though individually identified and set forth herein. Thus, the present invention contemplates each species separately and any and all combinations and permutations of species falling within Formula I.

The foregoing groups, as derived from the compounds listed above, may be C-attached or N-attached where such is possible. For instance, a group derived from pyrrole may be pyrrol-1-yl (N-attached) or pyrrol-3-yl (C-attached). The terms referring to the groups also encompass all possible tautomers.

As indicated, so-called 'prodrugs' of the compounds of Formula I are also within the scope of the invention. Thus certain derivatives of compounds of Formula I which may have little or no pharmacological activity themselves can, when administered into or onto the body, be converted into compounds of Formula I having the desired activity, for example, by hydrolytic cleavage. Such derivatives are referred to as 'prodrugs'. Further information on the use of prodrugs may be found in Pro-drugs as Novel Delivery Systems, Vol. 14, ACS Symposium Series (T. Higuchi and W. Stella) and Bioreversible Carriers in Drug Design, Pergamon Press, 1987 (Ed. E. B. Roche, American Pharmaceutical Association).

Prodrugs in accordance with the invention can, for example, be produced by replacing appropriate functionalities present in the compounds of Formula I with certain moieties known to those skilled in the art as 'pro-moieties' as described, for example, in Design of Prodrugs by H. Bundgaard (Elsevier, 1985).

Some examples of prodrugs in accordance with the invention include, but are not limited to,

(i) where the compound of Formula I contains a carboxylic acid functionality (-COOH), an ester thereof, for example, a compound wherein the hydrogen of the carboxylic acid functionality of the compound of Formula (I) is replaced by (C_1-C_8)alkyl;

(ii) where the compound of Formula I contains an alcohol functionality (-OH), an ether thereof, for example, a compound wherein the hydrogen of the alcohol functionality of the compound of Formula I is replaced by (C_1-C_6)alkanoyloxymethyl; and

(iii) where the compound of Formula I contains a primary or secondary amino functionality (-NH_2 or -NHR where R ≠ H), an amide thereof, for example, a compound wherein, as the case may be, one or both hydrogens of the amino functionality of the compound of Formula I is/are replaced by (C_1-C_{10})alkanoyl.

Further examples of replacement groups in accordance with the foregoing examples and examples of other prodrug types may be found in the aforementioned references.

Moreover, certain compounds of Formula I may themselves act as prodrugs of other compounds of Formula I.

Also included within the scope of the invention are metabolites of compounds of Formula I, that is, compounds formed *in vivo* upon administration of the drug. Some examples of metabolites in accordance with the invention include, but are not limited to,

(i) where the compound of Formula I contains a methyl group, an hydroxymethyl derivative thereof (-CH_3 -> -CH_2OH):

(ii) where the compound of Formula I contains an alkoxy group, an hydroxy derivative thereof (-OR -> -OH);

(iii) where the compound of Formula I contains a tertiary amino group, a secondary amino derivative thereof (-NR^1R^2 -> -NHR^1 or -NHR^2);

(iv) where the compound of Formula I contains a secondary amino group, a primary derivative thereof (-NHR^1 -> -NH_2);

(v) where the compound of Formula I contains a phenyl moiety, a phenol derivative thereof (-Ph -> -PhOH); and

(vi) where the compound of Formula I contains an amide group, a carboxylic acid derivative thereof (-$CONH_2$ -> COOH).

Compounds of Formula I containing one or more asymmetric carbon atoms can exist as two or more stereoisomers. Where a compound of Formula I contains an alkenyl or alkenylene group, geometric *cis/trans* (or Z/E) isomers are possible. Where structural isomers are interconvertible *via* a low energy barrier, tautomeric isomerism ('tautomerism') can occur. This can take the form of proton tautomerism in compounds of Formula I containing, for example, an imino, keto, or oxime group, or so-called valence tautomerism in compounds which contain an aromatic moiety. It follows that a single compound may exhibit more than one type of isomerism.

Included within the scope of the present invention are all stereoisomers, geometric isomers and tautomeric forms of the compounds of Formula I, including compounds exhibiting more than one type of isomerism, and mixtures of one or more thereof. Also included are acid addition or base salts wherein the counterion is optically active, for example, *d*-lactate or *l*-lysine, or racemic, for example, *dl*-tartrate or *dl*-arginine.

Cis/trans isomers may be separated by conventional techniques well known to those skilled in the art, for example, chromatography and fractional crystallisation.

Conventional techniques for the preparation/isolation of individual enantiomers include chiral synthesis from a suitable optically pure precursor or resolution of the racemate (or the racemate of a salt or derivative) using, for example, chiral high pressure liquid chromatography (HPLC).

Alternatively, the racemate (or a racemic precursor) may be reacted with a suitable optically active compound, for example, an alcohol, or, in the case where the compound of Formula I contains an acidic or basic moiety, a base or acid such as 1-phenylethylamine or tartaric acid. The resulting diastereomeric mixture may be separated by chromatography and/or fractional crystallization and one or both of the diastereoisomers converted to the corresponding pure enantiomer(s) by means well known to a skilled person.

Chiral compounds of the invention (and chiral precursors thereof) may be obtained in enantiomerically-enriched form using chromatography, typically HPLC, on an asymmetric resin with a mobile phase consisting of a hydrocarbon, typically heptane or hexane, containing from 0 to 50% by volume of isopropanol, typically from 2% to 20%, and from 0 to 5% by volume of an alkylamine, typically 0.1% diethylamine. Concentration of the eluate affords the enriched mixture.

When any racemate crystallises, crystals of two different types are possible. The first type is the racemic compound (true racemate) referred to above wherein one homogeneous form of crystal is produced containing both enantiomers in equimolar amounts. The second type is the racemic mixture or conglomerate wherein two forms of crystal are produced in equimolar amounts each comprising a single enantiomer.

While both of the crystal forms present in a racemic mixture have identical physical properties, they may have different physical properties compared to the true racemate. Racemic mixtures may be separated by conventional techniques known to those skilled in the art - see, for example, Stereochemistry of Organic Compounds by E. L. Eliel and S. H. Wilen (Wiley, 1994).

The present invention includes all pharmaceutically acceptable isotopically-labelled compounds of Formula I wherein one or more atoms are replaced by atoms having the same atomic number, but an atomic mass or mass number different from the atomic mass or mass number which predominates in nature.

Examples of isotopes suitable for inclusion in the compounds of the invention include, but are not limited to, isotopes of hydrogen, such as ^{2}H and ^{3}H, carbon, such as ^{11}C, ^{13}C and ^{14}C, chlorine, such as ^{36}Cl, fluorine, such as ^{18}F, iodine, such as ^{123}I and ^{125}I, nitrogen, such as ^{13}N and ^{15}N, oxygen, such as ^{15}O, ^{17}O and ^{18}O, phosphorus, such as ^{32}P, and sulphur, such as ^{35}S.

Certain isotopically-labelled compounds of Formula I, for example, those incorporating a radioactive isotope, are useful in drug and/or substrate tissue distribution studies. The radioactive isotopes tritium, *i.e.* ^{3}H, and carbon-14, *i.e.* ^{14}C, are particularly useful for this purpose in view of their ease of incorporation and ready means of detection.

Substitution with heavier isotopes such as deuterium, *i.e.* ^{2}H, may afford certain therapeutic advantages resulting from greater metabolic stability, for example, increased *in vivo* half-life or reduced dosage requirements, and hence may be preferred in some circumstances.

Substitution with positron emitting isotopes, such as ^{11}C, ^{18}F, ^{15}O and ^{13}N, can be useful in Positron Emission Topography (PET) studies for examining substrate receptor occupancy.

Isotopically-labeled compounds of Formula I can generally be prepared by conventional techniques known to those skilled in the art or by processes analogous to those described in the accompanying Examples and Preparations using an appropriate isotopically-labeled reagent in place of the non-labeled reagent previously employed.

Pharmaceutically acceptable solvates in accordance with the invention include those wherein the solvent of crystallization may be isotopically substituted, *e.g.* D_2O, d_6-acetone, d_6-DMSO.

Specific embodiments of the present invention include the compounds exemplified in the Examples below and the pharmaceutically acceptable salts thereof, complexes thereof, and derivatives thereof that convert into a pharmaceutically active compound upon administration:

Compounds of Formula I of this invention, and their pharmaceutically acceptable salts, have useful pharmaceutical and medicinal properties. The compounds of Formula I, and their pharmaceutically acceptable salts inhibit the production of Aβ-peptide (thus, gamma-secretase activity) in mammals, including humans. Compounds of Formula I, and their pharmaceutically acceptable salts, are therefore able to function as therapeutic agents in the treatment of the neurodegenerative and/or neurological disorders and diseases representatively enumerated below, for example Alzheimer's disease, in an afflicted mammal, including a human.

The present invention also relates to a pharmaceutical composition for inhibiting Aβ-peptide production in a mammal, including a human, comprising an amount of a compound of

Formula I, or a pharmaceutically acceptable salt thereof, that is effective in inhibiting Aβ-production, and a pharmaceutically acceptable carrier.

The present invention also relates to a pharmaceutical composition for treating a disease or condition selected from the group consisting of Alzheimer's disease, hereditary cerebral hemorrhage with amyloidosis, cerebral amyloid angiopathy, a prion-mediated disease, inclusion body myositis, stroke, multiple sclerosis, head trauma, mild cognitive impairment and Down's Syndrome in a mammal, including a human, comprising an amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof, that is effective in inhibiting Aβ-peptide production, and a pharmaceutically acceptable carrier.

The present invention also relates to a pharmaceutical composition for treating a disease or condition selected from the group consisting of Alzheimer's disease and Down's Syndrome in a mammal, including a human, comprising an amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof, that is effective in inhibiting Aβ-peptide production, and a pharmaceutically acceptable carrier.

The present invention also relates to a pharmaceutical composition for treating a disease or a condition selected from the group consisting of Alzheimer's disease, hereditary cerebral hemorrhage with amyloidosis, cerebral amyloid angiopathy, a prion-mediated disease, inclusion body myositis, stroke, multiple sclerosis, head trauma, mild cognitive impairment and Down's Syndrome in a mammal, including a human, comprising an amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof, that is effective in treating such disease or condition, and a pharmaceutically acceptable carrier.

The present invention also relates to a pharmaceutical composition for treating a disease or a condition selected from the group consisting of Alzheimer's disease and Down's Syndrome in a mammal, including a human, comprising an amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof, that is effective in treating such disease or condition, and a pharmaceutically acceptable carrier.

The present invention also relates to a method of inhibiting Aβ-peptide production in a mammal, including a human, comprising administering to said mammal an amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof, that is effective in inhibiting Aβ-production.

The present invention also relates to a method of treating a disease or condition selected from Alzheimer's disease, hereditary cerebral hemorrhage with amyloidosis, cerebral amyloid angiopathy, a prion-mediated disease, inclusion body myositis, stroke, multiple sclerosis, head trauma, mild cognitive impairment and Down's Syndrome in a mammal, including a human, comprising administering to said mammal an amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof, that is effective in inhibiting Aβ-production.

The present invention also relates to a method of treating a disease or condition selected from Alzheimer's disease and Down's Syndrome in a mammal, including a human, comprising administering to said mammal an amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof, that is effective in inhibiting Aβ-production.

The present invention also relates to a method of treating a disease or condition selected from Alzheimer's disease, hereditary cerebral hemorrhage with amyloidosis, cerebral amyloid angiopathy, a prion-mediated disease, inclusion body myositis, stroke, multiple sclerosis, head trauma, mild cognitive impairment and Down's Syndrome in a mammal, including a human, comprising administering to said mammal an amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof, that is effective in treating such condition.

The present invention also relates to a method of treating a disease or condition selected from Alzheimer's disease and Down's Syndrome in a mammal, including a human, comprising administering to said mammal an amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof, that is effective in treating such condition.

The compounds of Formula I may be used alone or used in combination with any other drug, including, but not limited to, any memory enhancement agent, *e.g.,* Aricept™ and/or Namenda™, antidepressant agent, *e.g.,* Zoloft™, anxiolytic, antipsychotic agent, *e.g.,* Geodon™, sleep disorder agent, anti-inflammatory agent, *e.g.,* Celebrex™, Bextra™, etc., anti-oxidant agent, cholesterol modulating agent (for example, an agent that lowers LDL or increases HDL), *e.g.,* Lipitor™, Caduet™, etc., Histamine (H2) antagonist, *e.g.,* Cimetadine™, and anti-hypertension agent, *e.g.,* Norvasc™, Caduet™, etc. Accordingly, the present invention also relates to the following pharmaceutical compositions and methods of treatment comprising a compound of Formula I in combination with other drugs, such as those of the type described above.

The present invention also relates to a pharmaceutical composition for treating a disease or condition associated with Aβ-peptide production in a mammal, including a human, comprising (a) a compound of Formula I, or a pharmaceutically acceptable salt thereof; (b) a memory enhancement agent, *e.g.,* Aricept™ and/or Namenda™, antidepressant, *e.g.,* Zoloft™, anxiolytic, antipsychotic agent, *e.g.,* Geodon™, sleep disorder agent, anti-inflammatory agent, *e.g.,* Celebrex™, Bextra™, etc., anti-oxidant agent, cholesterol modulating agent (for example, an agent that lowers LDL or increases HDL), *e.g.,* Lipitor™, Caduet™, etc., Histamine (H2) antagonist, *e.g.,* Cimetadine™, and anti-hypertensive agent, *e.g.,* Norvasc™, Caduet™, etc.; and (c) a pharmaceutically acceptable carrier; wherein the active agents "a" and "b" above are present in amounts that render the composition effective in treating such disease or condition.

The present invention also relates to a pharmaceutical composition for treating a disease or condition selected from the group consisting of Alzheimer's disease, hereditary

cerebral hemorrhage with amyloidosis, cerebral amyloid angiopathy, a prion-mediated disease, inclusion body myositis, stroke, multiple sclerosis, head trauma, mild cognitive impairment and Down's Syndrome, in a mammal, including a human, comprising (a) a compound of Formula I, or a pharmaceutically acceptable salt thereof; (b) a memory enhancement agent, *e.g.,* Aricept™ and/or Namenda™, antidepressant, *e.g.,* Zoloft™, anxiolytic, antipsychotic agent, *e.g.,* Geodon™, sleep disorder agent, anti-inflammatory agent, *e.g.,* Celebrex™, Bextra™, etc., anti-oxidant agent, cholesterol modulating agent (for example, an agent that lowers LDL or increases HDL), *e.g.,* Lipitor™, Caduet™, etc., Histamine (H2) antagonist, *e.g.,* Cimetadine™, and anti-hypertensive agent, *e.g.,* Norvasc™, Caduet™, etc.; and (c) a pharmaceutically acceptable carrier; wherein the active agents "a" and "b" above are present in amounts that render the composition effective in treating such disease or condition.

The present invention also relates to a pharmaceutical composition for treating a disease or condition selected from the group consisting of Alzheimer's disease and Down's Syndrome, in a mammal, including a human, comprising (a) a compound of Formula I, or a pharmaceutically acceptable salt thereof; (b) a memory enhancement agent, *e.g.,* Aricept™ and/or Namenda™, antidepressant, *e.g.,* Zoloft™, anxiolytic, antipsychotic agent, *e.g.,* Geodon™, sleep disorder agent, anti-inflammatory agent, *e.g.,* Celebrex™, Bextra™, etc., anti-oxidant agent, cholesterol modulating agent (for example, an agent that lowers LDL or increases HDL), *e.g.,* Lipitor™, Caduet™, etc., Histamine (H2) antagonist, *e.g.,* Cimetadine™, and anti-hypertensive agent, *e.g.,* Norvasc™, Caduet™, etc.; and (c) a pharmaceutically acceptable carrier; wherein the active agents "a" and "b" above are present in amounts that render the composition effective in treating such disease or condition.

The present invention also relates to a method of treating a disease or condition associated with Aβ-peptide production in a mammal, including a human, comprising administering to said mammal (a) a compound of Formula I, or a pharmaceutically acceptable salt thereof; and (b) a memory enhancement agent, *e.g.,* Aricept™ and/or Namenda™, antidepressant, *e.g.,* Zoloft™, anxiolytic, antipsychotic agent, *e.g.,* Geodon™, sleep disorder agent, anti-inflammatory agent, *e.g.,* Celebrex™, Bextra™, etc., anti-oxidant agent, cholesterol modulating agent (for example, an agent that lowers LDL or increases HDL), *e.g.,* Lipitor™, Caduet™, etc., Histamine (H2) antagonist, *e.g.,* Cimetadine™, and anti-hypertensive agent, *e.g.,* Norvasc™, Caduet™, etc.; wherein the active agents "a" and "b" above are present in amounts that render the composition effective in treating such disease or condition.

The present invention also relates to a method of treating a disease or condition selected from the group consisting of Alzheimer's disease, hereditary cerebral hemorrhage with amyloidosis, cerebral amyloid angiopathy, a prion-mediated disease, inclusion body myositis, stroke, multiple sclerosis, head trauma, mild cognitive impairment and Down's

Syndrome, in a mammal, including a human, comprising administering to said mammal (a) a compound of Formula I, or a pharmaceutically acceptable salt thereof; and (b) a memory enhancement agent, *e.g.,* Aricept™ and/or Namenda™, antidepressant, *e.g.,* Zoloft™, anxiolytic, antipsychotic agent, *e.g.,* Geodon™, sleep disorder agent, anti-inflammatory agent, *e.g.,* Celebrex™, Bextra™, etc., anti-oxidant agent, cholesterol modulating agent (for example, an agent that lowers LDL or increases HDL), *e.g.,* Lipitor™, Caduet™, etc., Histamine (H2) antagonist, *e.g.,* Cimetadine™, and anti-hypertensive agent, *e.g.,* Norvasc™, Caduet™, etc.; wherein the active agents "a" and "b" above are present in amounts that render the composition effective in treating such disease or condition.

The present invention also relates to a method of treating a disease or condition selected from the group consisting of Alzheimer's disease and Down's Syndrome, in a mammal, including a human, comprising administering to said mammal (a) a compound of Formula I, or a pharmaceutically acceptable salt thereof; and (b) a memory enhancement agent, *e.g.,* Aricept™ and/or Namenda™, antidepressant, *e.g.,* Zoloft™, anxiolytic, antipsychotic agent, *e.g.,* Geodon™, sleep disorder agent, anti-inflammatory agent, *e.g.,* Celebrex™, Bextra™, etc., anti-oxidant agent, cholesterol modulating agent (for example, an agent that lowers LDL or increases HDL), *e.g.,* Lipitor™, Caduet™, etc., Histamine (H2) antagonist, *e.g.,* Cimetadine™, and anti-hypertensive agent, *e.g.,* Novasc™; Caduet™, etc.; wherein the active agents "a" and "b" above are present in amounts that render the composition effective in treating such disease or condition.

Compounds of Formula I, or any of the combinations described in the immediately preceding paragraphs, may optionally be used in conjunction with a known P-glycoprotein inhibitor, such as verapamil.

References herein to diseases and conditions "associated with Aβ-peptide production" relate to diseases or conditions that are caused, at least in part, by Aβ-peptide and/or the production thereof. Thus, Aβ-peptide is a contributing factor, but not necessarily the only contributing factor, to "a disease or condition associated with Aβ-peptide production."

The compounds of Formula I, or their pharmaceutically acceptable salts may also be used to modulate or inhibit the Notch signaling pathway in organisms, including humans. The Notch signaling pathway is an evolutionarily conserved mechanism utilized by organisms, ranging from worms through humans, to regulate fate determination of various cell lineages. Notch belongs to the family of epidermal growth factor-like homeotic genes, which encode transmembrane proteins with variable numbers of epidermal growth factor-like repeats in the extracellular domain. There is increasing evidence for a role of the Notch pathway in human disease. All of the components of the pathway have yet to be identified, but among those

identified to date, mutations that affect their interaction with each other can lead to a variety of syndromes and pathological conditions.

For example, Notch signaling is typically associated with cell fate decision. The finding that Notch activation stimulates capillary outgrowth suggests that Notch receptors must be activated to allow this process to occur. Therefore, Notch modulation provides a method for regulating angiogenesis. Specifically, modulation of Notch signaling can be used to modulate angiogenesis (e.g., by blocking Notch signaling to block angiogenesis). This inhibition of angiogenesis in vivo can be used as a therapeutic means to treat a variety of diseases, including but not limited to cancer, diabetic retinopathy, rheumatoid arthritis, psoriasis, inflammatory bowel disease and arteriosclerosis.

The Notch pathway is also implicated in the development and maturation of T cells, as described in Radtke, F. et al., Immunity 10:547-558, 1999. The compounds of Formula I, and their pharmaceutically acceptable salts are therefore useful candidates for modulating the immune system, including the treatment of inflamamation, asthma, graft rejection, graft versus host disease, autoimmune disease and transplant rejection.

In addition, a number of studies published between 2002 and 2004 have provided convincing evidence that Notch signaling is frequently elevated in a variety of human tumors (including, but not limited to breast, prostate, pancreas and T-cell acute lymphoblastic leukemia). One key study provides a strong genetic link to Notch's role in important tumor types. Specifically, Weijzen et al. demonstrated that Notch signaling maintains the neoplastic phenotype in human Ras-transformed cells. Weijzen et al. (2002) *Nature Med* 8: 979. Because 30% of human malignancies may carry activating mutations in at least one of the three isoforms of Ras, this finding raises the possibility that Notch inhibitors would be a powerful addition to anti-cancer therapy. Another study's findings support a central role for aberrant Notch signaling in the pathogenesis of human T cell acute lymphoblastic leukemia/lymphoma. Pear et al., *Current Opinion in Hematology* (2004), 11(6), 426-433.

Accordingly, the compounds of Formula I, or their pharmaceutically acceptable salts, may be used for treating a disease or condition selected from the group consisting of cancer, arteriosclerosis, diabetic retinopathy, rheumatoid arthritis, psoriasis, inflammatory bowel disease inflammation, asthma, graft rejection, graft versus host disease, autoimmune disease and transplant rejection.

As used herein, the term "treating" refers to reversing, alleviating or inhibiting the progress of a disease, disorder or condition, or one or more symptoms of such disease, disorder or condition, to which such term applies. As used herein, "treating" may also refer to decreasing the probability or incidence of the occurrence of a disease, disorder or condition in a mammal as compared to an untreated control population, or as compared to the same mammal prior to treatment. For example, as used herein, "treating" may refer to preventing a

disease, disorder or condition, and may include delaying or preventing the onset of a disease, disorder or condition, or delaying or preventing the symptoms associated with a disease, disorder or condition. As used herein, "treating" may also refer to reducing the severity of a disease, disorder or condition or symptoms associated with such disease, disorder or condition prior to a mammal's affliction with the disease, disorder or condition. Such prevention or reduction of the severity of a disease, disorder or condition prior to affliction relates to the administration of the composition of the present invention, as described herein, to a subject that is not at the time of administration afflicted with the disease, disorder or condition. As used herein "treating" may also refer to preventing the recurrence of a disease, disorder or condition or of one or more symptoms associated with such disease, disorder or condition. The terms "treatment" and "therapeutically," as used herein, refer to the act of treating, as "treating" is defined above.

Compounds of Formula I, and their pharmaceutically acceptable salts, may be prepared as described in the following reaction Schemes and discussion. Unless otherwise indicated, as referred to in the reaction schemes and discussion that follow, R^1, R^2, R^3, R^4, R^6, R^7, R^8, R^9, R^{10}, R^{11}, A, Z and n are as defined above.

The compounds of Formula I may have asymmetric carbon atoms and may therefore exist as racemic mixtures, diasteroisomers, or as individual optical isomers.

Separation of a mixture of isomers of compounds of Formula I into single isomers may be accomplished according to conventional methods known in the art.

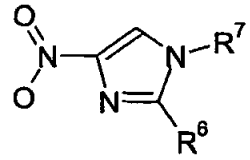
The compounds of Formula I may be prepared by the methods described below, together with synthetic methods known in the art of organic chemistry, or modifications and derivatisations that are familiar to those of ordinary skill in the art. Preferred methods include, but are not limited to, those described below.

The reactions described below are performed in solvents that are appropriate to the reagents and materials employed and that are suitable for use in the reactions described. In the description of the synthetic methods described below, it is also to be understood that all reaction conditions, whether actual or proposed, including choice of solvent, reaction temperature, reaction duration time, reaction pressure, and other reaction conditions (such as anhydrous conditions, under argon, under nitrogen, etc.), and work up procedures, are those conditions that are standard for that reaction, as would be readily recognized by one of skill in the art. Alternate methods may also be used.

Compounds of formula II wherein R^7 contains an alcohol moiety may be oxidized using standard oxidation method known in art, such as, e.g., Dess-Martin reagents, Swern oxidation, or use of SO_3-pyridine, CrO_3, to provide compounds of formula II wherein R^7 contains a ketone or aldehyde. Compounds of formula II wherein R^7 is a ketone or aldehyde may convert to the corresponding compounds of formula II wherein R^7 is an imine (by

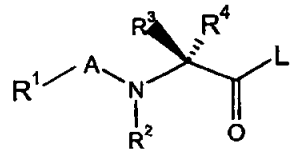
reaction with an amine), olefin (by a Wittig reaction), alcohol (by a Grignard reaction), or other derivative (by standard reactions).

The compounds of formula I of the present invention and their salts can be prepared by a reaction process comprising a compound of formula II



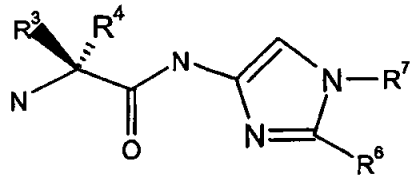
(II)

with a compound of formula III



(III)

or reacting a compound of formula IV



(IV)

with a compound of formula V



(V)

wherein R^1, R^3, R^4, R^6, R^7, and A are as defined above and L is hydroxy or a suitable leaving group. If desired, the 4-amino-imidazole derivative of formula I or synthetic intermediate of formula IV may be converted into a salt by methods known to those of ordinary skill in the art.

Examples of specific compounds of formula III and V wherein L is hydroxy or a suitable leaving group are those wherein L represents a halogen atom, such as Cl, Br, or I, or A-L is an alkyl or aryl ester.

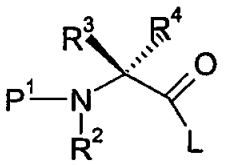
Compounds in formula I can be prepared by reacting a compound of formula II and a carboxylic acid of formula III, or a compound of formula IV with a compound of formula V. Compounds of formula IV can be prepared by reacting a compound of formula II with a compound of formula VI.

The reaction between compounds of formula II and compounds of formula III, between compounds of formula IV and compounds of formula V, and between compounds of

formula II and compounds of formula VI, can be carried out by standard methods. For example, wherein L is a hydroxy group, these reactions can be carried out in the presence of a coupling agent or a polymer supported coupling agent, such as, for example, carbodiimide, i.e. 1,3-dicyclohexylcarbodiimide (DCC), 1,3-diisopropylcarbodiimide, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDC), N-cyclohexylcarbodiimide, or N'-methylpolystyrene in the presence or absence of HOBt, in a suitable solvent such as , for instance, a single solvent or a combination of several solvents selected from dichloromethane (CH_2Cl_2), chloroform ($CHCl_3$), tetrahydrofuran (THF), diethyl ether (Et_2O), 1,4-dioxane, acetonitrile, (CH_3CN), toluene, N,N-dimethylformamide (DMF), or dimethylsulfoxide (DMSO), at a suitable temperature such as from about –10°C to about reflux, for a suitable time monitored by chromatography or LC-MS. An alternative method wherein L is OH is carried out by converting OH to a leaving group by reaction with oxalyl chloride, thionyl chloride or a mixed anhydride method, using an alkyl chloroformate, such as C_1-C_4 alkyl chloroformate, in the presence of a base such as triethylamine, N,N-diisopropylethylamine, pyridine, or dimethylaminopyridine, in a suitable solvent such as, for example, methylene chloride, chloroform, tetrahydrofuran (THF), toluene, diethyl ether, acetonitrile, 1,4-dioxane, n,N-dimethylformamide, dimethylsulfoxide (DMSO), N-methyl pyrrolidinone (NMP), or xylene, at a temperature of from about –30°C to about room temperature.

Alternatively, aminoimidazole coupling may be achieved as follows. A compound of formula I may be prepared by coupling an amino-imidazole II with III wherein C(=O)L is an ester, in the presence of trialkylaluminium preferably trimethylaluminum in an appropriate solvent such as methylene chloride, THF, dioxane, toluene, etc., at an appropriate temperature, such as from about room temperature to about reflux, or in a sealed reactor (such as sealed tube or inscrewed vials). Similarly, compound IV may be prepared by reacting an amino-imidazole II, triamethylaluminum and N-Boc of an alpha-amino acid ester, followed by removal of the Boc group using standard methods.

The protected amino compounds of formula VI, where P^1 is a blocking group such as an N-Boc group, can be prepared by methods well known in the literature, for example the methods described in Theodora W. Greene's book "Protective Groups in Organic Synthesis". Compounds of formula IV can be prepared in an analogous method as above by reacting compound of formula II with a compound of formula VI, followed by deblocking the P^1 group. Deprotection can be performed by well-known methods, for example when P^1 is N-Boc, removal by any methods well-known in the literature, for example HCl(g) in an appropriate solvent such as 1,4-dioxane, diethylether or trifluoroacetic acid in methylene chloride. Many other amino protecting groups are known and may also be used, such as benzyl or *p*-methoxy-benzyl, trimethylsilyl, *t*-butyldimethylsilyl, etc. Methods for deblocking such groups are also well-known in the literature and may be used.



(VI)

The compounds of formula II, III, IV, V and VI, in certain circumstances, are known compounds or can be obtained according to methods well known to one of skill in the art.

Compounds of formula III and V, wherein L is a leaving group as defined above, can be obtained according to conventional methods from the corresponding carboxylic acids of formula III where X is hydroxy.

Compounds of formula IV can be prepared by reacting a compound of formula II with a compound of formula V using known methods.

An ester group of R^7 in compounds of formula I or II may be converted to the corresponding amide using a similar method for amide bond formation, preferably employing trimethylaluminum in an appropriate solvent or a mixture of solvents, such as THF/toluene.

A keto group of R^7 in compounds of formula I or II may be converted to the corresponding amine using a well-established reductive amination method by reacting such ketone with an appropriate amine, with or without acid catalyst/ammonium acetate/dry agents (such as anhydrous Na_2SO_4 or $MgSO_4$), and a reducing agent, such as sodium triacetoxy borohydride, sodium cyanoborohydride, or sodium borohydride, or the corresponding polymer bound-$NaBH_4$, polymer bound-$NaBH_3CN$, or polymer bound-$NaB(OAc)_3H$, or any reducing agent (e.g., hydrogenation) that is known in the literature for reducing an imine bond to an amine, in an appropriate solvent, such as dichloroethane, chloroform, THF, MeOH, ethanol, isopropanol, *t*-butanol or toluene, at a temperature from about room temperature to about reflux, preferably from about room temperature to about 65°C.

Compounds wherein R^6 is a halo group may be generated by reacting the starting material wherein R^6 is H with NBS (N-bromosuccinamide), NCS (N-chlorosuccinamide), or SO_2Cl_2, I_2 in an appropriate solvent such as methylene chloride, carbontetrachloride or chloroform. The halo group may then be replaced with another group using methods known in the art, such as halogen-metal exchange, followed by quenching with an electrophile, or using typical Suzuki coupling conditions employing a catalyst such as a palladium complex, e.g., tetrakis(triphenylphosphine)-palladium, with sodium carbonate as a base, in a suitable solvent such as THF, DME, or ethanol, and a boronic acid.

4-amino-imidazole II may be prepared by the following methods known in the chemical literature (e. g., Tetrahedron, **1995**, *51*, 2875-2894; J. Chem. Soc. Perkin 1, **1987**, 2819-2828; Bull. Chem. Soc. Fr. **1994**, 131, 200-209; Tetrahedron Lett. **1996**, 4423-4426; Tetrahedron **1996**, 37, 4423-4426; Tetrahedron, **1994**, *50*, 5741-5752; Heterocycles, **1994**,

37, 1511-1520; Tetrahedron Lett. **1999**, 1623-1626; Organic Lett. 2002, 4, 4133-4134; Organic Lett. 2000, 2, 1233-1236; J. Med. Chem. 1990, 33, 1091-1097;or by the methods described below.

Scheme 1 illustrates methods suitable for preparing amino-imidazole compounds of formula **I**. Referring to Scheme 1, treatment of a solution of 1,4-dinitroimidazole (*J. Phys. Chem.* (1995) Vol. 99, pp. 5009-5015) in dimethylsulfoxide (DMSO), pyridine-water, water, an alcohol, or an alcohol-water solvent system, but preferably in a lower alcohol such as methanol, from about –20°C to about 50°C, preferably from about –5°C to 35°C, with a primary alkyl or aryl amine (NR^9R^{10}) affords 1-*N*-substituted-4-nitroimidazoles of formula 2A. 1,4-dinitroimidazole is a highly energetic, semi-stable substance and should be stored in a freezer at all times it is not in use. Thermodynamic measurements have shown that it can potentially generate enough energy at 35°C under adiabatic conditions to violently explode. Extreme caution should be exercised at all time using this material. Reduction of the nitro compound of formula **2A** to the amine of formula **3A** may be accomplished by exposing a mixture of a compound of formula **2A** and a noble metal catalyst, in a solvent such as ethyl acetate, tetrahydrofuran, dioxane, or a mixture thereof, to an atmosphere of hydrogen gas at a pressure of about 1 to 100 atmospheres, where a preferred pressure of hygrogen gas is about one to about ten atmospheres. Palladium is the preferred noble metal catalyst. The metal may be conveniently suspended on an inert solid support such as charcoal and filtered to provide the amine of formula **3A**.. Alternatively, the nitro group of formula **2A** to the amine of formula **3A** may be accomplished by exposing a mixture of a compound of formula **2A** to zinc/HCl or iron/HCl or with $NaBH_4/NiCl_2$ or with $NaBH_2S_3$.

The resulting amine of formula **3A** is reacted immediately with an acid chloride, acid anhydride, or an activated carboxylic acid derivative (defined by Formula **III**), in the presence of a base, such as triethylamine, diisopropylethylamine, pyridine, or 2,6-lutidine, from about –78°C to 40°C. The reaction between compounds of formula **3A** and compounds of formula **III** can be carried out by standard methods. For example, wherein L of formula **III** is a hydroxy group, these reactions can be carried out in the presence of a coupling agent or a polymer supported coupling agent, such as, for example, carbodiimide, i.e. 1,3-dicyclohexylcarbodiimide (DCC), 1,3-diisopropylcarbodiimide, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDC), N-cyclohexylcarbodiimide, or N'-methylpolystyrene in the presence or absence of HOBt, in a suitable solvent such as , for instance, a single solvent or a combination of several solvents selected from dichloromethane (CH_2Cl_2), chloroform ($CHCl_3$), tetrahydrofuran (THF), diethyl ether (Et_2O), 1,4-dioxane, acetonitrile, (CH_3CN), toluene, N,N-dimethylformamide (DMF), or dimethylsulfoxide (DMSO), at a suitable temperature such as from about –10°C to about reflux, for a suitable time monitored by chromatography or LC-MS. An alternative method wherein L is OH is carried out by converting OH to a leaving group by

reaction with oxalyl chloride, thionyl chloride or a mixed anhydride method, using an alkyl chloroformate, such as C_1-C_4 alkyl chloroformate, in the presence of a base such as triethylamine, N,N-diisopropylethylamine, pyridine, or dimethylaminopyridine, in a suitable solvent such as, for example, methylene chloride, chloroform, tetrahydrofuran (THF), toluene, diethyl ether, acetonitrile, 1,4-dioxane, N,N-dimethylformamide, dimethylsulfoxide (DMSO), N-methyl pyrrolidinone (NMP), or xylene, at a temperature of from about –30°C to about room temperature.

Alternatively, aminoimidazole coupling may be achieved as follows. A compound of formula **I** may be prepared by coupling an amino-imidazole **3A** with a compound of formula **III** wherein C(=O)L is an ester, in the presence of trialkylaluminium preferably trimethylaluminum in an appropriate solvent such as methylene chloride, THF, dioxane, toluene, etc., at an appropriate temperature, such as from about room temperature to about reflux, or in a sealed reactor (such as sealed tube or inscrewed vials).

Alternatively, the resulting amine of formula **3A** is reacted immediately with an acid chloride, acid anhydride, or an activated carboxylic acid derivative (defined by Formula **IV**), in the presence of a base, such as triethylamine, diisopropylethylamine, pyridine, or 2,6-lutidine, from about –78°C to 40°C to form a compound of formula **4A**. The reaction between compounds of formula **3A** and compounds of formula **IV** can be carried out by standard methods. For example, wherein L of formula **IV** is a hydroxy group, these reactions can be carried out in the presence of a coupling agent or a polymer supported coupling agent, such as, for example, carbodiimide, i.e. 1,3-dicyclohexylcarbodiimide (DCC), 1,3-diisopropylcarbodiimide, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDC), N-cyclohexylcarbodiimide, or N'-methylpolystyrene in the presence or absence of HOBt, in a suitable solvent such as , for instance, a single solvent or a combination of several solvents selected from dichloromethane (CH_2Cl_2), chloroform ($CHCl_3$), tetrahydrofuran (THF), diethyl ether (Et_2O), 1,4-dioxane, acetonitrile, (CH_3CN), toluene, N,N-dimethylformamide (DMF), or dimethylsulfoxide (DMSO), at a suitable temperature such as from about –10°C to about reflux, for a suitable time monitored by chromatography or LC-MS. An alternative method wherein L is OH is carried out by converting OH to a leaving group by reaction with oxalyl chloride, thionyl chloride or a mixed anhydride method, using an alkyl chloroformate, such as C_1-C_4 alkyl chloroformate, in the presence of a base such as triethylamine, N,N-diisopropylethylamine, pyridine, or dimethylaminopyridine, in a suitable solvent such as, for example, methylene chloride, chloroform, tetrahydrofuran (THF), toluene, diethyl ether, acetonitrile, 1,4-dioxane, N,N-dimethylformamide, dimethylsulfoxide (DMSO), N-methyl pyrrolidinone (NMP), or xylene, at a temperature of from about –30°C to about room temperature.

Alternatively, aminoimidazole coupling may be achieved as follows. A compound of formula **4A** may be prepared by coupling an amino-imidazole **3A** with a compound of formula **IV** wherein C(=O)L is an ester, in the presence of trialkylaluminium preferably trimethylaluminum in an appropriate solvent such as methylene chloride, THF, dioxane, toluene, etc., at an appropriate temperature, such as from about room temperature to about reflux, or in a sealed reactor (such as sealed tube or inscrewed vials). The protected amino compounds defined as PG, such as a compound with an Boc group, of formula **IV** can be prepared by methods well known in the literature, for example the methods described in Theodora W. Greene's book "Protective Groups in Organic Synthesis".

Compounds defined as by Formula **5A** can be prepared from compounds of formula **4A** by deblocking the PG group. Deprotection can be performed by well-known methods, for example when PG is N-Boc, removal by any methods well-known in the literature, for example HCl(g) in an appropriate solvent such as 1,4-dioxane, diethylether or trifluoroacetic acid in methylene chloride. Many other amino protecting groups are known and may also be used, such as benzyl or *p*-methoxy-benzyl, trimethylsilyl, *t*-butyldimethylsilyl, etc. Methods for deblocking such groups are also well-known in the literature and may be used.

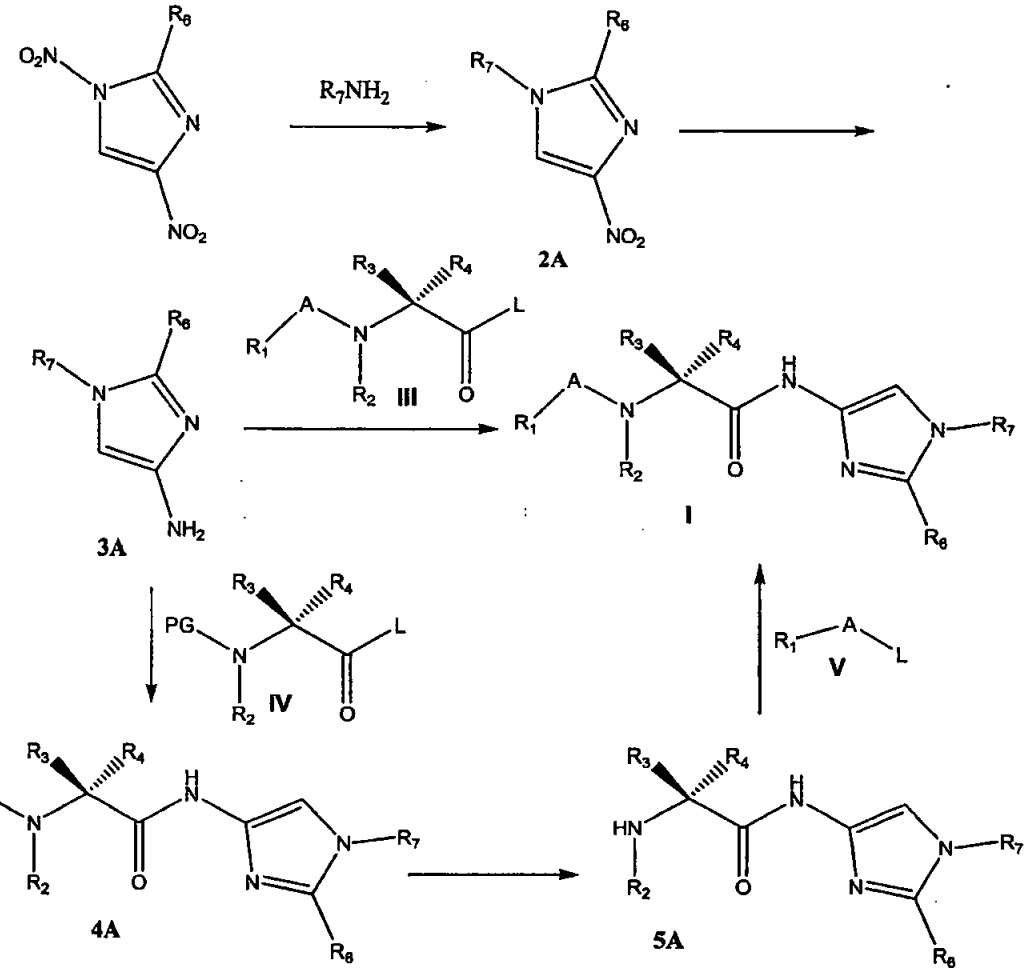
Compounds of Formula I can be formed by reaction between compounds of formula **5A** and compounds of formula **V** can be carried out by standard methods. For example, wherein L is a hydroxy group, these reactions can be carried out in the presence of a coupling agent or a polymer supported coupling agent, such as, for example, carbodiimide, i.e. 1,3-dicyclohexylcarbodiimide (DCC), 1,3-diisopropylcarbodiimide, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDC), N-cyclohexylcarbodiimide, or N'-methylpolystyrene in the presence or absence of HOBt, in a suitable solvent such as , for instance, a single solvent or a combination of several solvents selected from dichloromethane (CH_2Cl_2), chloroform ($CHCl_3$), tetrahydrofuran (THF), diethyl ether (Et_2O), 1,4-dioxane, acetonitrile, (CH_3CN), toluene, N,N-dimethylformamide (DMF), or dimethylsulfoxide (DMSO), at a suitable temperature such as from about –10°C to about reflux, for a suitable time monitored by chromatography or LC-MS. An alternative method wherein L is OH is carried out by converting OH to a leaving group by reaction with oxalyl chloride, thionyl chloride or a mixed anhydride method, using an alkyl chloroformate, such as C_1-C_4 alkyl chloroformate, in the presence of a base such as triethylamine, N,N-diisopropylethylamine, pyridine, or dimethylaminopyridine, in a suitable solvent such as, for example, methylene chloride, chloroform, tetrahydrofuran (THF), toluene, diethyl ether, acetonitrile, 1,4-dioxane, n,N-dimethylformamide, dimethylsulfoxide (DMSO), N-methyl pyrrolidinone (NMP), or xylene, at a temperature of from about –30°C to about room temperature.

Alternatively, aminoimidazole coupling may be achieved as follows. A compound of formula **I** may be prepared by coupling an amino-imidazole **5A** with **V** wherein L is an ester, in

the presence of trialkylaluminium preferably trimethylaluminum in an appropriate solvent such as methylene chloride, THF, dioxane, toluene, etc., at an appropriate temperature, such as from about room temperature to about reflux, or in a sealed reactor (such as sealed tube or inscrewed vials).

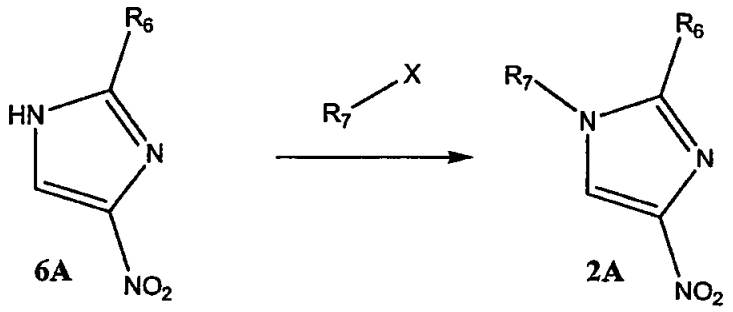
Alternatively, compounds of Formula I can be formed by reaction between compounds of formula **5A** and compounds of formula **V** when L is an aldehyde or ketone by using a well-established reductive amination method by reacting such ketone or aldehyde with an appropriate amine **5A**, with or without acid catalyst/ammonium acetate/dry agents (such as anhydrous Na_2SO_4 or $MgSO_4$), and a reducing agent, such as sodium triacetoxy borohydride, sodium cyanoborohydride, or sodium borohydride, or the corresponding polymer bound-$NaBH_4$, polymer bound-$NaBH_3CN$, or polymer bound-$NaB(OAc)_3H$, or any reducing agent (e.g., hydrogenation) that is known in the literature for reducing an imine bond to an amine, in an appropriate solvent, such as dichloroethane, chloroform, THF, MeOH, ethanol, isopropanol, *t*-butanol or toluene, at a temperature from about room temperature to about reflux, preferably from about room temperature to about 65°C.

Scheme 1



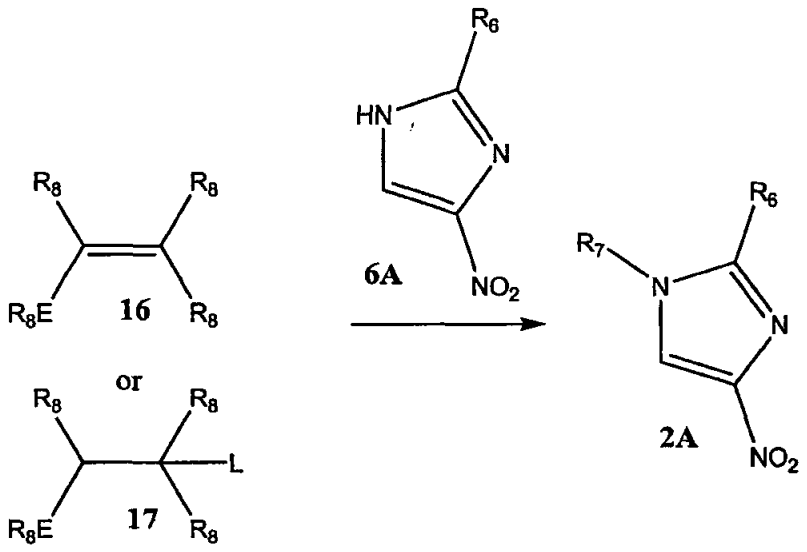
Scheme 2 illustrates additional methods for the synthesis of imidazole compounds defined as Formula **2A**. Treatment of nitroimidazole **6A** with a base such as sodium hydride, potassium hydride, alkyl lithium, alkoxides, in a solvent such as tetrahydrofuran, dimethylformamide, methylene chloride, ether, preferably dimethylformamide, from about –60°C to 40°C, where from –10°C to 20°C is preferred, followed by addition of R7-X wherein X is defined as Cl, Br, I, F, alkylsulfonate, or arylsulfonate followed by warming the reaction from 23 °C to 150°C where 30-80°C is preferrable, affords imidazoles of formula **2A**. Reduction of the nitro compound and coupling reaction is carried out in a similar manner described above and is useful for preparing compounds of Formula I. Alternatively, R7 can be further functionalized by procedures described within or using methods known to one skilled in the art.

Scheme 2



Scheme 3 illustrates additional methods for the synthesis of nitro-imidazole compounds defined as Formula **2A**. A key starting material for the synthesis is the double-bond compound (a compound of Formula **16** or **17**) substituted with the group ER8 and one to three groups selected from R^8, where ER8 is defined as an electron-withdrawing group chosen from $C(=O)R^9$, $C(=O)OR^9$, $C9=O)NR^9R^{10}$, $S(=O)_2R^9$, $S(=O)_2$ NR^9R^{10}, $S(=O)_2OR^9$, cyano, and heteroaryl. Additionally, compounds of formula **16** or **17** may be defined wherein ER8 is connected to one of the groups R^8 or directly to the carbon-carbon double bond to form a ring and thus includes comopunds such as 2-cyclopentene-1-one and 2-cyclohexene-1-one. Alternatively, compounds of formula **17** where L is defined as Cl, Br, I, $OC(=O)R^9$, or $OS(=O)_2R^9$ may be used as starting materials; examples of such compounds are 3-chloro-1-cyclopentanone, 3-acetoxy-1-cyclobutanone. Thus, referring to Scheme 3, treatment of -= 4-nitroimidazole **6A**, with a base such as sodium hydride, potassium hydride, cesium carbonate, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or tetraalkylammonium chloride, where DBU is the preferred base, with intermediates **16** or **17**, in a solvent such as acetonitrile, methylene chloride, 1,2-dichloroethane, or chloroform, where acetonitrile is the preferred solvent, at a temperature from about –60 °C to about 50 °C, where –20 °C to 23 °C is the preferred range, affords addition products of formula **2A**. Reduction of the nitro compound and coupling to give compounds of formula **I** is carried out in a similar manner described above.

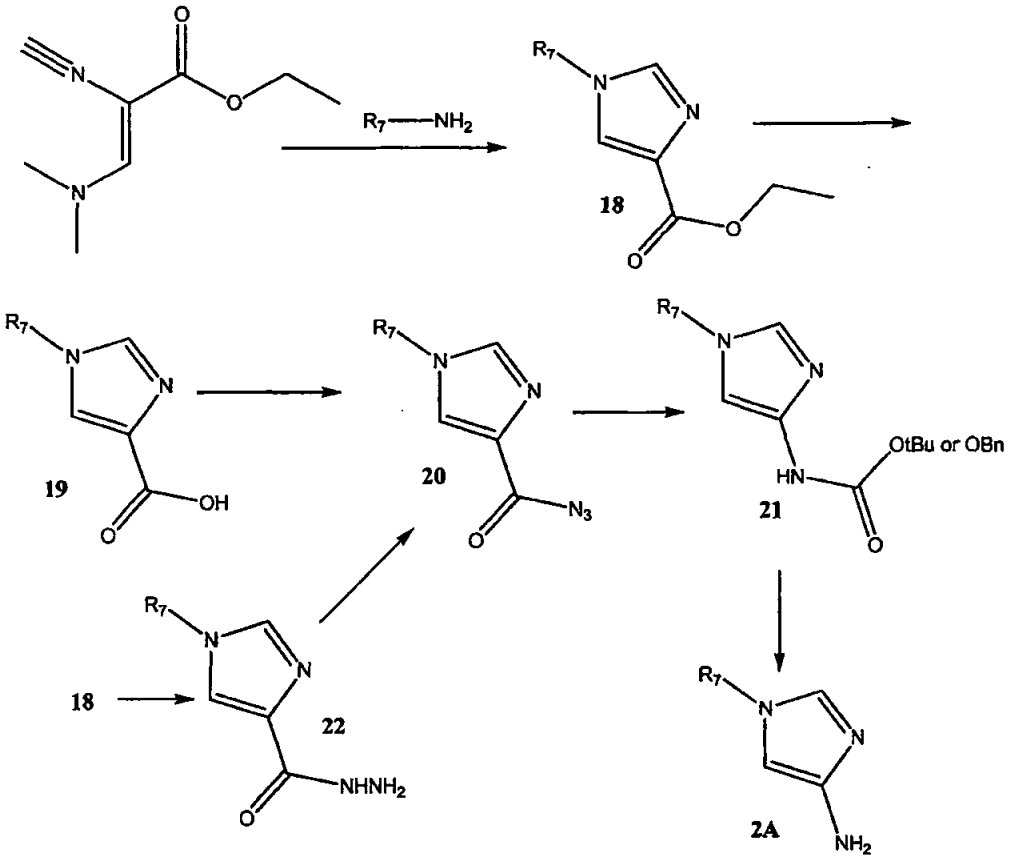
Scheme 3



Scheme 4 below illustrates additional methods for the synthesis of amino-imidazole compounds defined as Formula **2A**. Treatment of ethyl-2-isocyano-3-*N*,*N*-dimethylamino acrylate or benzyl-2-isocyano-3-*N*-*N*-dimethylamino acrylate with a primary amine, R7-NH2, in a solvent such as *n*-butanol, *n*-propanol, *I*-propanol, or ethanol, or in the absence of solvent, where *n*-propanol or no solvent are preferred, from about 23 °C to about 200 °C, where from about 60 °C to 150 °C is preferred, affords imidazoles of formula **18**. Treatment of ester **18** with a base such as potasium hydroxide, lithium hydroxide, or sodium hydroxide in a - solvent such as tetrahydrofuran, water, methanol, ethanol, propanol, wherein methanol is preferred provides the acid **19**. The acid is converted to the acylazide **20** using methods known to one skilled in the art such as treatment of acid **19** with thionyl chloride or oxalyl chloride from –20 to 50 °C followed by removal of the residual solvent and quenching with sodium or potassium azide in a solvent such as toluene, tetrahydrofuran, methlene chloride, dioxane. The azide **20** undergoes Curtius rearrangement to the Boc **21** by heating from 5 °C -200 °C in a solvent such as *t*-butanol, benzyl alcohol, and ethanol. If t-butanol is used, deprotection of the N-Boc protecting group can be accomplished with HCl or triflouroacetic acid in a solvent such as ether, tetrahydrofuran, where HCl in methanol is preferred affords the desired aminoimidazole compounds of formula **2A**. If benzyl alcohol is used, deprotection can be accomplished by the use of a noble metal catalyst, in a solvent such as ethyl acetate, tetrahydrofuran, dioxane, or a mixture thereof, to an atmosphere of hydrogen gas at a pressure of about 1 to 100 atmospheres, where a preferred pressure of hygrogen gas is about one to about ten atmospheres. Palladium is the preferred noble metal catalyst which affords the desired aminoimidazole compounds of formula **2A**. Alternatively, ester **18** can be treated with hydrazine in a solvent such as water from a temperature from 50 °C to 200 °C where 80 °C to 120 °C is preferred provides the hydrazide **22**. The hydrazide **22** can be converted to the

acylazide **20** using *t*-butylnitrite in a solvent or combination of solvent such as ether, methylene chloride, dichloroethane, chloroform, where in ether/methylene chloride is preferred at a temperature from –50 °C to 23 °C wherein –30 °C to 10 °C is preferred. The acylazide is then converted onto aminoimidazole compounds of formula **2A** as described above.

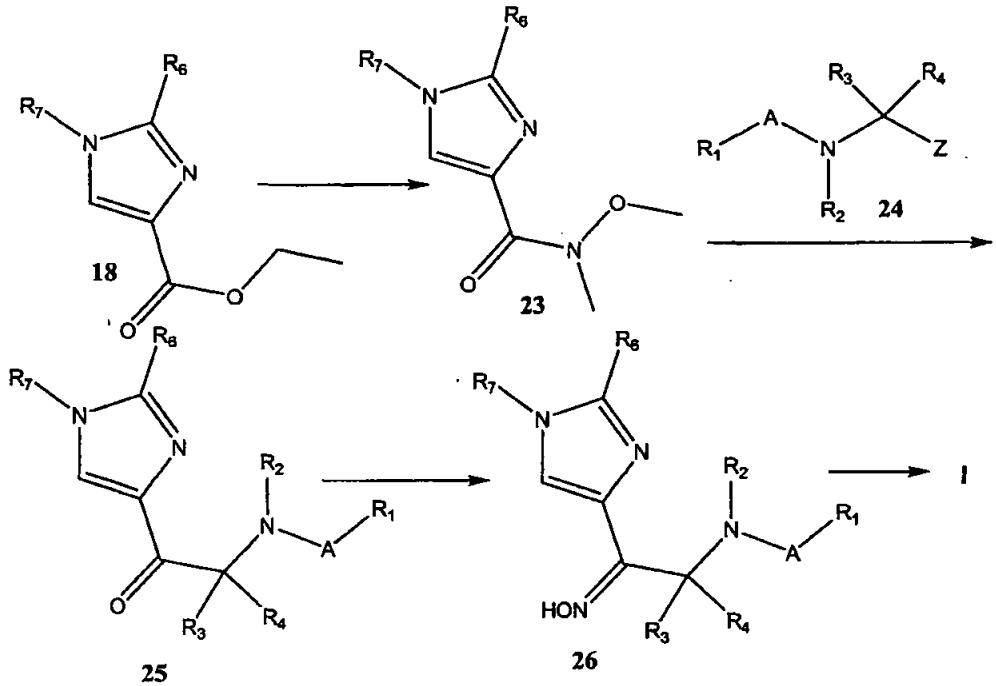
Scheme 4



Scheme 5 below illustrates additional methods for the synthesis of amino-imidazole compounds defined as Formula **I**. Treatment of N-O-dimethyl hydroxyl amine hydrochloride with trimethylaluminum in 1,2-dichloroethane followed by the addition of ester **18**, prepared as described above and heating at about 30 °C to about 80 °C, where a temperature of about 50 °C is preferred, affords imidazole **23**. Addition of an organometallic reagent **24** wherein Z is defined as lithium halide, magnessium halide, potassium halide, where lithium halide is preferred, to a solution of amide **23** in a solvent such as tetrahydrofuran, methylene chloride, or diethyl ether, from a temperature about –78 °C to about 30 °C, where a range of about –20 °C to about 0 °C is preferred affords **25**. Addition of **25** to a mixture of hydroxyl amine hydrochloride and potassium acetate in a lower alcoholic solvent, where in ethanol is preferred, at about 23°C, yields oxime **26** as a mixture of isomers. Treatment of an acetone solution of oxime **26** at about 0°C with aqueous hydroxide followed by paratoluenesulfonyl chloride yields a mixture of O-sulfonyl compound following extractive workup. Dissolution of the crude material in a non-polar

solvent such as benzene, hexanes, or toluene, wherein benzene is preferred, and application to a column of alumina followed by elution with chloroform-methanol (about 10:1) after approximately five minutes provides a compound of Formula **I**.

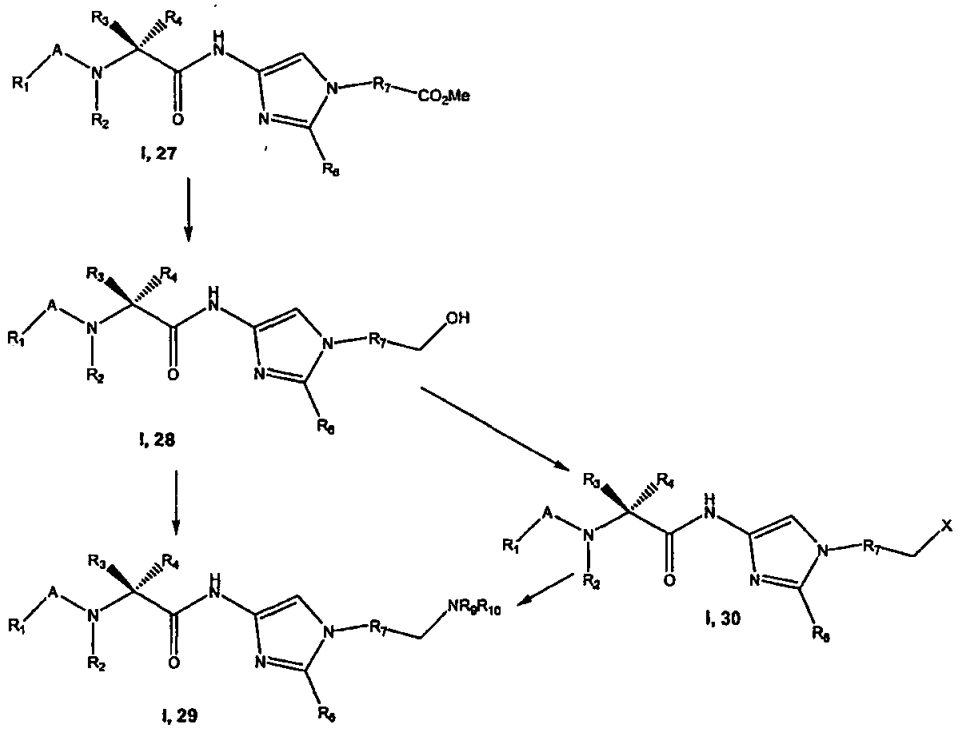
Scheme 5



Scheme 6 illustrates methods suitable for preparing amino-imidazole compounds of formula **I**. Compound of Formula **I, 27** can be prepared using methods described above. Converstion of ester **I, 27** to alcohol of compounds **I, 28** can be accomplished by treatment of ester **I, 27** with an appropriate reducing agent such as sodium borohydride or lithium aluminum hydride using conditions well known to one skilled in the art. Compounds of formula **I, 28** may be oxidized using standard oxidation method known in art, such as, e.g., Dess-Martin reagents, Swern oxidation, or use of SO_3-pyridine, CrO_3,, where Swern oxidation is preferred to provide compounds containing an aldehyde. The aldehyde can be converted onto compounds of formula **I, 29** using well-established reductive amination method by reacting the aldehyde with an appropriate amine **5A**, with or without acid catalyst/ammonium acetate/dry agents (such as anhydrous Na_2SO_4 or $MgSO_4$), and a reducing agent, such as sodium triacetoxy borohydride, sodium cyanoborohydride, or sodium borohydride, or the corresponding polymer bound-$NaBH_4$, polymer bound-$NaBH_3CN$, or polymer bound-$NaB(OAc)_3H$, or any reducing agent (e.g., hydrogenation) that is known in the literature for reducing an imine bond to an amine, in an appropriate solvent, such as dichloroethane, chloroform, THF, MeOH, ethanol, isopropanol, *t*-butanol or toluene, at a temperature from about room temperature to about reflux, preferably from about room temperature to about

65°C. Alternatively, the alcohol of **I, 28** can be converted to the corresponding alkyl or aryl sulfonate **I, 30** by treatment of the alcohol with alkyl or aryl sulfonyl chloride (where in mesyl chloride is preferred) in a solvent such as methylene chloride, tetrahydrofuran, toluene wherein methylene chloride in the presence of an amide such as triethylamine, diisopropyamine, pyridine, 2,6-lutidine, where in triethylamine is preferred at a temperature from –50 °C to 23 °C wherein –0 °C to 30 °C is preferred. The aryl or alkyl sulfonate is then reacted with an alkali metal azide (wherein sodium azide is preferred), in a polar solvent such as dimethylformamide, dimethylsulfoxide, alcohol, wherein ethanol is preferred produces a compound containing an azide. This intermediate azide may be reduced by exposing the azide to a noble metal catalyst, in a solvent such as ethyl acetate, tetrahydrofuran, dioxane, or a mixture thereof, to an atmosphere of hydrogen gas at a pressure of about 1 to 100 atmospheres, where a preferred pressure of hygrogen gas is about one to about ten atmospheres. Palladium is the preferred noble metal catalyst and the reaction affords the amine group. The amine group can then be converted to compounds of Formula **1, 29** using the reductive amination conditions described above.

Scheme 6

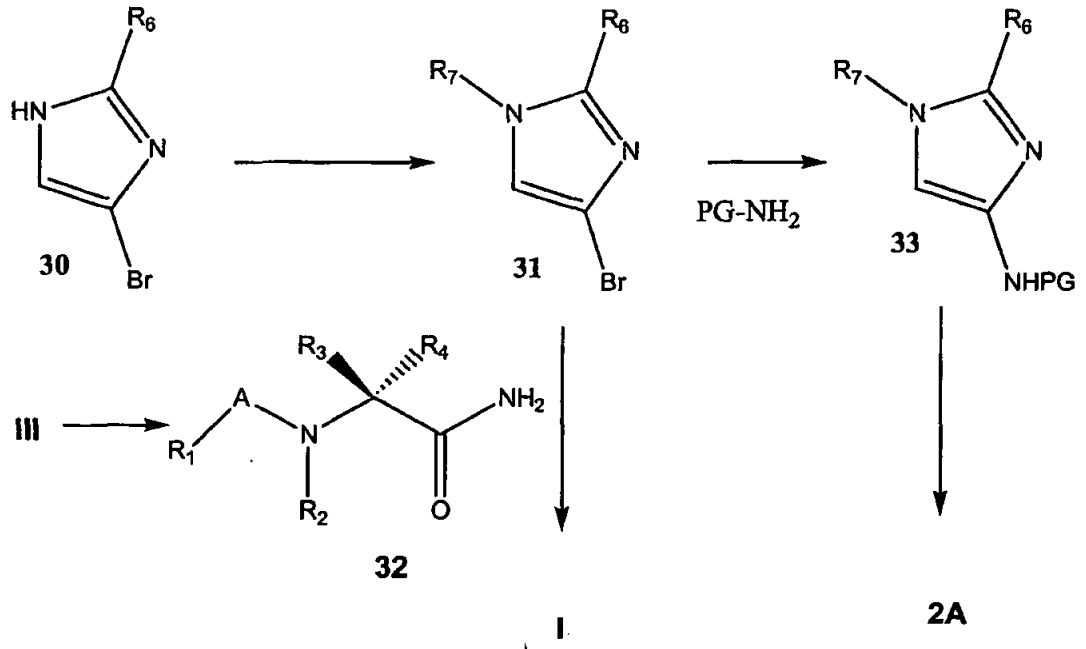


Referring to Scheme 7, treatment of a solution of bromoimidazole **30** with a base, such as sodium hydride, potassium hydride, lithium hydride, cesium carbonate, sodium hydroxide, potassium hydroxide, cesium hydroxide, lithium diisopropyl amide, sodium amide, potassium hexamethyldisilazide, sodium hexamethyldisilazide, sodium *tert*-butoxide, or potassium *tert*-butoxide, in a reaction inert solvent such as tetrahydrofuran, 1,4-dioxane, *N,N*-

dimethylformamide, dimethylsulfoxide, or toluene, from about –20 °C to 150 °C, where 20 °C to 100 °C is preferred, in the absence or presence of a phase transfer catalyst, such as *tetra-n*-butylammonium chloride, *tetra-n*-butylammonium bromide, *tetra-n*-butylammonium iodide, benzyltrimethyl ammonium chloride, benzyltrimethyl ammonium bromide, or benzyltrimethyl ammonium fluoride, followed by the addition of an alkyl, allylic, or benzylic chloride, bromide, iodide, alkyl sulfonate, aryl sulfonate, or triflate, affords imidazoles **31**.

Treatment of 1-substituted-4-bromoimidazole (**31**) with an intermediate of the formula **32** or PG-NH2 (where PG is defined as (C=O)alkyl or benzoyl) and a palladium catalyst such as palladium (II) acetate, allyl palladium chloride dimer, tris(dibenzylideneacetone)dipalladium (0), tris(dibenzylideneacetone)dipalladium (0) chloroform adduct, or palladium (II) chloride, where palladium (II) acetate, tris(dibenzylideneacetone)dipalladium (0), and tris(dibenzylideneacetone)dipalladium (0) chloroform adduct are preferred, and a phosphine ligand, preferably 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene (XANTPHOS) is preferred, and a base, such as cesium carbonate, or potassium phosphate (K_3PO_4), where potassium phosphate is preferred, in a reaction inert solvent, such as toluene, 1,4-dioxane, or tetrahydrofuran, from about 0 °C to 150 °C, where 20 °C to 110 °C is preferred, affords the coupled product 1. Alternatively, treatment of 1-substituted-4-bromoimidazole (**31**) with an intermediate of the formula **32** or PG-NH2 (where PG is defined as (C=O)alkyl or benzoyl) and a diamine, such as 1,2-ethylenediamine, *N,N'*-dimethylethylenediamine, or cis-1,2-diaminocyclohexane, preferably *N,N'*-dimethylethylenediamine, and cuprous chloride, bromide or iodide, preferably cuprous iodide, in the presence of a small amount of water, preferably about 1% to about 4% water, in a reaction inert solvent such as 1,2-dimethoxyethane, diglyme, t-butyl methyl ether, tetrahydrofuran, benzene or toluene, preferably toluene, at a temperature of about 40°C to about 150°C, preferably about 80°C to about 120 °C to yield the compound of formula **I** or compounds of formula **33**. In the case of compound **33**, this can be converted to compounds of forumla **2A** using standard methods described above.

Scheme 7



The starting materials used in the procedures of the above Schemes, the syntheses of which are not described above, are either commercially available, known in the art or readily obtainable from known compounds using methods that will be apparent to those skilled in the art.

The compounds of Formula I, and the intermediates shown in the above reaction schemes, may be isolated and purified by conventional procedures, such as recrystallization or chromatographic separation, such as on silica gel, either with an ethyl acetate/hexane elution gradient, a methylene chloride/methanol elution gradient, or a chloroform/methanol elution gradient. Alternatively, a reverse phase preparative HPLC or chiral HPLC separation technique may be used.

In each of the reactions discussed or illustrated above, pressure is not critical unless otherwise indicated. Pressures from about 0.5 atmospheres to about 5 atmospheres are generally acceptable, and ambient pressure, *i.e.*, about 1 atmosphere, is preferred as a matter of convenience.

The compounds of Formula I of the present invention are useful in inhibiting Aβ-peptide production (thus, gamma-secretase activity) in mammals, and therefore they are able to function as therapeutic agents in the treatment of the aforementioned disorders and diseases in an afflicted mammal.

A specific compound of Formula I can be determined to inhibit Aβ-peptide production using biological assays known to those of ordinary skill in the art, for example the assays described below.

For testing efficacy in vitro, the effect of test compounds on the secretion of Aß from cells in tissue culture was determined. H4 cells (human brain neuroglioma) were stably transfected with human APP695 containing the Swedish Familial Alzheimers Disease mutation. Cells were distributed into 96-well plates at a density of about 30,000 cells/well and allowed to attach to the plate surface for approximately 6 hours at 37°C. After this time, cells were washed to remove secreted Aβ and fresh media containing test compound was added. Following incubation with compound overnight at 37°C, media was harvested and subjected to immunoassay to determine the amount of Aβ secreted from the cells. Various assays for Aβ peptides known to those skilled in the art can be applied to these samples for quantitation of Aβ secretion. In this application, a two-site sandwich ELISA utilizing commercially available monoclonal antibodies, 6E10 and 4G8-biotinylated, were employed to provide an estimate of the amount of most of the physiologically relevant forms of Aβ, e.g., Aβ1-40, Aβ1-42. Signals from these samples were compared to standard curves generated with synthetic Aβ1-40 peptide and used to calculate IC_{50} values for each test compound.

Using such assay, compounds of the present invention were determined to have an IC_{50} activity for inhibiting gamma-secretase activity of less than about 800 micromolar. Preferred compounds of the invention are compounds that were determined to have an IC_{50} activity for inhibiting gamma-secretase activity of less than about 1 micromolar.

The following Examples illustrate the present invention. It is to be understood, however, that the invention, as fully described herein and as recited in the claims, is not intended to be limited by the details of the following Examples.

Examples

General Procedure A:

Coupling method for amide formation

a) EDC/ HOBt/trialkylamine Coupling Procedure

A mixture of a carboxylic acid (1.0 e.q.), amine (1.0 e.q.), HOBt (1.1-1.5 eq.), EDC (1.2-1.8 eq.) and a trialkylamine (triethylamine or diisopropylethylamine) (3-6 eq.) in an appropriate solvent or a mixture of solvents, for example methylene chloride, dichloroethane, THF, or DMF, was stirred at room temperature until product formation or disappearance of starting material. The solvent was removed under reduced pressure, the residue taken up in ethyl acetate (or similar selected solvent such as methylene chloride or chloroform) and water. The organic layer was separated, washed with dilute HCl (if the desired product contains a basic functional group, washing with dilute HCl may be omitted), brine, and dried over sodium sulfate. The solvent was then removed at reduced pressure to provide product.

b) HATU/ trialkylamine Coupling Procedure

A mixture of a carboxylic acid (1.0 e.q.), amine (1.0 e.q.), HATU (1.1-1.5 eq.) and a trialkylamine (triethylamine or diisopropylethylamine) (3-6 eq.) in an appropriate solvent or a

mixture of solvents, for example methylene chloride, dichloroethane, THF, or DMF, was stirred at room temperature until product formation or disappearance of starting material. The solvent was removed under reduced pressure, the residue taken up in ethyl acetate (or similar selected solvent such as methylene chloride or chloroform) and water. The organic layer was separated, washed with dilute HCl (if the desired product contains a basic functional group, washing with dilute HCl may be omitted), brine, and dried over sodium sulfate. The solvent was then removed at reduced pressure to provide product.

c) PyBOP/ trialkylamine Coupling Procedure

A mixture of a carboxylic acid (1.0 e.q.), amine (1.0 e.q.), PyBOP (1.1-1.5 eq.) and a trialkylamine (triethylamine or diisopropylethylamine) (3-6 eq.) in an appropriate solvent or a mixture of solvents, for example methylene chloride, dichloroethane, THF, or DMF, was stirred at room temperature until product formation or disappearance of starting material. The solvent was removed under reduced pressure, the residue taken up in ethyl acetate (or similar selected solvent such as methylene chloride or chloroform) and water. The organic layer was separated, washed with dilute HCl (if the desired product contains a basic functional group, washing with dilute HCl may be omitted), brine, and dried over sodium sulfate. The solvent was removed at reduced pressure to provide product.

d) HBTU/trialkylamine Coupling Procedure

A mixture of a carboxylic acid (1.0 e.q.), amine (1.0 e.q.), HBTU (1.1-1.5 eq.), and a trialkylamine (triethylamine or diisopropylethylamine) (3-6 eq.) in an appropriate solvent or a mixture of solvents, for example methylene chloride, dichloroethane, THF, or DMF, was stirred at room temperature until product formation or disappearance of starting material. The solvent was removed under reduced pressure, the residue taken up in ethyl acetate (or similar selected solvent such as methylene chloride or chloroform) and water. The organic layer was separated, washed with dilute HCl (if the desired product contains a basic functional group, washing with dilute HCl may be omitted), brine, and dried over sodium sulfate. The solvent was removed at reduced pressure to provide product.

e) Chloro-alkylformate Coupling Procedure

A mixture of a carboxylic acid (1 eq.) and triethylamine (eq.) was dissolved in an appropriate solvent, such as DMF and cooled to –23°C. *Iso*-butyl formate (1 eq.) was added dropwise with stirring. After stirring for a period of time (form 15 min to 2 hr), a 2-amino-thiazole or an amine (1 eq.) was added and stirring continued for an additional 30 min at –23°C. The mixture was then warmed to room temperature until amide formation (typically overnight). The mixture was quenched with water and brine and extracted with an appropriate solvent such as ethyl acetate, methylene chloride or chlorform. The organic layer was washed with dilute $NaHSO_4$, $NaHCO_3$ and brine and the solvent was removed under reduced pressure to provide product. Purification may be necessary.

f) TPTU Coupling Procedure

To the acid (1 equiv) was suspended in dry DMF, Diisoproplyethyl amine (2-4 equiv) and TPTU (1 equiv) were added and the resulting mixture was stirred at room temperature for 1 to 2 hour. To an aliquot of this solution was added the appropriate amine and the mixture was stirred at room temperature over night. 1N NaOH was added and the resulting mixture was extracted with ethyl acetate. The organic extracts were loaded onto SCX SPE (Silicycle, 1g) which was washed with MeOH. The product was then eluted with 1N triethyl amine in MeOH and the resulting fraction was concentrated. Purification was on Waters XTerra PrepMS C18 OBD column (19 X 100mm) and provided the title compound. Gradient elution with water/ acetonitrile (18ml/min) with a 1% trifluoroacetic acid modifier (2ml/min).

General Procedure B:

Method for reductive amination

a) Sodium triacetoxyborohydride

An amine (1-4 eq.) in dichloroethane or THF was added to a solution of a ketone (1 eq.), $NaBH(OAc)_3$ (1-3 eq.) and acetic acid (1-3 eq.) in dichloroethane or THF. The mixture was stirred at room temperature until product formation or disappearance of starting material. The mixture was quenched with diluted base, extracted with methylene chloride or other appropriate solvent such as chloroform or ethyl acetate. The organic layer was separated, dried and concentrated to give the desired amide. Purification may be necessary.

b) Sodium cyanoborohydride

A mixture of a ketone or aldehyde (1 eq.), an amine (1-20 eq.), sodium cyanoborohydride (1-5 eq.), acetic acid (1-3 eq.), sodium acetate (1-3 eq.), anhydrous sodium sulfate in dichloroethane or THF was stirred at room temperature to 60°C, preferably heated at 35-50°C until product formation. The mixture was quenched with diluted base, extracted with methylene chloride or other appropriate solvent such as chloroform or ethyl acetate. The organic layer was separated, dried and concentrated to give the desired amide. Purification may be necessary.

c) Potassium Formate and Palladium Acetate

A solution of an aldehyde or a ketone (1 eq.) and an amine (1 eq.) in dry DMF was stirred at room temperature for 4 hr, in the presence of molecular sieves. To the resulting reaction mixture were added potassium formate (2 eq.) and palladium acetate (catalytic amount, 0.02 eq.). The mixture was heated at 40-60°C to complete reaction (TLC) and after cooling it was diluted with ice-water. The mixture was extracted with an appropriate solvent (such as methylene chloride, ethyl acetate, or chloroform). The organic layer was separated, dried and concentrated to give the desired amide. Purification may be necessary.

General Procedure C:

Sodium borohydride reduction of ketone or aldehyde

A mixture of an aldehyde or a ketone (1 eq.) and sodium borohydride (1 –10 eq.) in an appropriate solvent (methanol or ethanol) was stirred at 0°C to room temperature for 10 minutes to complete reaction (TLC). The mixture was concentrated to a small volume, quenched with water, extracted with an appropriate solvent (such as methylene chloride, ethyl acetate, or chloroform). The organic layer was separated, dried and concentrated to give the desired amide. Purification may be necessary.

General Procedure D:

N-tBOC deprotecting procedure

To a solution of N-tBOC compound in 1,4-dioxane (0.03-0.09 M) was added 4 N HCl in 1,4-dioxane or anhydrous HCl gas under nitrogen. The reaction mixture was stirred at room temperature for 1-24 hrs until all the starting material consumed (TLC). The solution was concentrated and pumped in vacuo. The final HCl salt of the corresponding amine was typically used without further purification.

General Procedure E:

Conjugate Addition to Nitroimidazole

To a suspension of 4-nitroimidazole (2.0 equiv.) in acetonitrile is added DBU (1.0 equiv) followed by enone (1.0 equiv.). The reaction is heated for 12-24 hrs and the solvent removed in vacuo. The resultant solids are removed by filtration with methylene chloride and the resultant oil concentrated and purified by silica gel chromatography to provide the desired nitroimidazole.

General Proceudre F:

Alkylation of Nitroimidazole using Sodium Hydride

To a suspension of 4-nitroimidazole (1.0 equiv.) in dimethylformamide at rt under a nitrogen atmosphere is added sodium hydride (1.2 equiv.) portionwise. The reaction is stirred for 15-30 min. And then the appropriate alkylhalide or alkyl mesylate is added. The mixture is stirred for 12-24h at 50°C, cooled to 0°C, and quenched with water. The aqueous layer is extrated with methylene chloride, dried, and purified by silica gel chromatography to provide the desired nitroimidazole.

Alkylation of Nitroimidazole using potassium carbonate

To a suspension of 4-nitroimidazole (1.0 equiv.) in dimethylformamide at rt under a nitrogen atmosphere is added potassium carbonate (1-4 equiv.) portionwise. The reaction is stirred for 15-30 min. And then the appropriate alkylhalide or alkyl mesylate is added. The mixture is stirred for 12-24h at 50°C to 90 °C, cooled to rt, and quenched with water. The aqueous layer is extrated with methylene chloride, dried, and purified by silica gel chromatography or recrystalized to provide the desired nitroimidazole.

General Procedure G:

Reduction of Nitroimidazole A

To a solution of the nitroimidazole (1.0 equiv.) in ethylacetate is added palladium on carbon (0.25 w/w%). The reaction is hydrogenated @ 40-60 psi for 2-6 hrs and filtered over a pad of celite using ethyl acetate. The majority of the ethylacetate is removed in vacuo and the solution of the amine in the remaining ethylacetate is used without further purification.

Reduction of Nitroimidazole B

A Parr bottle was charged with nitroimidazole (1 equiv), dioxane and (1-3 equiv) of Raney nickel which had been washed with water until the supernatant was at pH = 7. The mixture was placed under 50 psi of hydrogen pressure and shaken for 45 minutes. After filtration and evaporation, the product, was used directly in the next step without further purification.

General Procedure H:

Reduction of Nitroimidazole-ester followed by Reductive Amination

To a solution of appropriate ester such as 3-Methyl-3-(4-nitro-imidazol-1-yl)-butyric acid methyl ester (1.0 equiv.) in methylene chloride at –78 °C is added DIBAL (2 equiv.) dropwise. The reaction is stirred for 1h, quenched with ethylacetate, removed from cooling bath, and stirred for 10 min. To the reaction is added water and allowed to warm to rt and stir for 1h. The reaction is diluted with methylene chloride, Na_2SO_4 is added and the reaction filtered through celite. The solvent is removed to afford the aldehyde such as 2-Methyl-2-(4-nitro-imidazol-1-yl)-propionaldehyde which is used in the next step without further purification.

To a solution of the appropriate aldehyde such as 2-Methyl-2-(4-nitro-imidazol-1-yl)-propionaldehyde (1 equiv.) in methylene chloride is added an appropriate amine (2 equiv.) and 4A molecular sieves. The reaction is stirred for 4-6 hours and an appropriate hydride reducing agent such as sodium triacetoxyborohydride (2 equiv.) is added. The reaction is stirred for 6-24h, quenched with sodium bicarbonate, and the aqueous layer extracted with methylene chloride. The solvent is removed and residue purified by silica gel chromatography to provide the desired nitroimidazole.

General Procedure I:

Ester Reduction

To a solution of ester (1 equiv) in an appropriate solvent such as diethyl ether or tetrahydrofuran at –78 °C to 0°C is added lithium aluminum hydride (1 equiv) and the reaction is stirred at 0°C for 15 min and warmed to rt for 1h. The reaction is slowly quenched with water and ethyl acetate. The reaction is filtered and the aqueous is extracted with ethylacetate, dried, and concentrated. Alternatively, the reaction is quenched with water, 1N NaOH and water, stirred and filtered through celite. The filtrate was concentrated to dryness.

Using either workup, the resultant residue is purified by silica gel chromatography to provide the title alcohol.

General Procedure J

Swern Oxidation

To a solution of oxalyl chloride (1.2 equiv) in methylene chloride at -78°C is added DMSO (3 equiv) dropwiese. The reaction is stirred for 20 min. and the alcohol (1 equiv) is added in methylene chloride. The reaction is stirred for 1h, triethylamine (4-5 equiv) is added, and the reaction warmed to 0°C for 20 min to 2 hours. The reaction is quenched with 100 mL of sodium bicarbonate, extracted with methylene chloride, dried, and concentrated to afford the title compound.

Dess Martin Oxidation

A mixture of 1 eq. of an alcohol and 1 to 1.5 eq. of Dess-Martin oxidizing agent in methylene chloride (2 mL per mmole reaction) was stirred at rt until reaction done. The mixture was quenched with water, filtered. The organic layer was separated, dried and concentrated to give the corresponding aldehyde.

General Procedure K:

Epoxide Opening:

Isopropanol was added to the appropriate amine followed by the addition of Hunig's base (2 equiv) and the appropriate epoxide (1 equiv), the reaction mixture was heated at 60-100 °C overnight. The mixture was quenched with dilute aq bicarb solution and extracted with dichloromethane. The organic extracts were dried (Na_2SO_4) and concentrated to afford 200mg crude material which was purified on a silica get flash column to afford the desired compound.

General Procedure M:

Substitution of dinitroimidazole

A solution of (1 equiv) of 1,4-dinitro-1H-imidazole (WO99/08699) and appropriate amine (1-2 equiv) in 1:1 MeOH – water was stirred at room temperature for 48 hrs. The solvent was removed in vacuo. The residue was taken up in methylene chloride and chromatographed on silica gel to provide the desired compound.

General Procedure N:

Mesylate Formation (A)

The appropriate alcohol (1 equiv) was dissolved in pyridine and treated with methansulfonyl chloride (2.2 equiv) at 0°C. The reaction was warmed to rt and stirred for 4h, quenched with sodium bicarbonate, and extracted with methylene chloride. The extracts were dried and concentrated to provide the appropriate mesylate which was used without further purification.

Mesylate Formation (B)

To the appropriate alcohol (1 equiv), methanesulfonyl chloride (1 equiv), triethylamine (1 equiv) in methylene chloride was stirred at rt for 1 to 8 hr. The reaction mixture was quenched with waster, the organic layer was separated and concentrated to give the desired mesylate which was used without further purification.

General Procedure O:

Mesylate Displacement:

A 0.1 M solution of mesylate in acetonitrile was treated with 3 equiv. of amine and 3 equiv. of K_2CO_3 and heated at 65-80 C with stirring for 24-75 hrs. Once judged complete by APCI or TLC, the reaction was quenched with H_2O and extracted with DCM. Silica gel chromatography or HPLC afforded pure product in 30-75% yield.

General Procedure P:

Benzyl Halide Displacement:

A 0.1 M solution of imidazole in DMF was treated with 1.1-2.1 equiv of benzyl halide and 2.1 equiv of K_2CO_3 and heated at 65 C with stirring for 18-30 hrs. In some cases, reaction was facilitated by the addition of 0.05 equiv of Et_3NBnCl. Once judged complete by APCI or TLC, the reaction was quenched with H_2O and extracted with EtOAc. The combined extracts were washed with H_2O and brine, dried over $MgSO_4$, filtered and concentrated. Alternatively, reactions were worked up by extraction with DCM. Extracts were loaded onto an SCX SPE (1 g, Silicycle) cartridge. After washing with MeOH, crude product was eluted with 1 N TEA in MeOH. Silica gel chromatography or HPLC afforded pure product in 30-75% yield.

General Proceudre R:

Ester Hydrolysis

The ester (1 equiv) is dissolved in THF:water (5:1) and LiOH (1.2 equiv) is added. The reaction is stirred overnight at rt, the solvent is removed, water added, and the pH is adjusted to 7 using 1N hydrochloric acid. The solid is filtered, washed with water and diethyl ether, and dried to afford the desired acid.

The following intermediates were prepared by methods analogous to those described above for General Method F;

1-(3-Methyl-oxetan-3-ylmethyl)-4-nitro-1H-imidazole; H1 NMR, (400 MHz), CDCl3) δ 1.25 (s, 3 H), 4.28 (s, 2 H), 4.42 (dd, J = 6.6 Hz, 37.3 Hz, 4 H), 7.44 (s, 1 H), 7.80 (s, 1 H).

4-Nitro-1-[1-(4-trifluoromethyl-phenyl)-ethyl]-1H-imidazole: H1 NMR, (400 MHz), CDCl3): δ 1.96 (d, 3 H), 5.49 (q, 1 H), 7.33 (d, 2 H), 7.53 (s, 1 H), 7.67 (d, 2 H), 7.78 (s, 1 H).

1-Benzyl-4-nitro-1H-imidazole; was prepared according to the procedure of Searcey, M.; Pye, P. L.; Lee, J. B.; Synth. Commun.; EN; 19; 7,8; 1989; 1309-1316.

1-(4-Nitro-imidazol-1-yl)-cyclobutanecarboxylic acid methyl ester; MS 240 m/z (M+1).

2-(4-Nitro-imidazol-1-yl)-cyclobutanecarboxylic acid methyl ester; MS 240 m/z (M+1).

The following intermediates were prepared from dinitroimidazole by methods analogous to those described above for General Method M;

1-Indan-1-yl-4-nitro-1H-imidazole; MS 230 m/z (M+1).

(1R,2S)-(1-(4-Nitro-imidazol-1-yl)-indan-2-ol; MS 246 m/z (M+1).

(1S,2R)-(1-(4-Nitro-imidazol-1-yl)-indan-2-ol; MS 246 m/z (M+1).

2-(4-fluorophenyl)-2-(4-nitro-1H-imidazol-1-yl)ethanol; MS 252 m/z (M+1).

(2-(4-nitro-1H-imidazol-1-yl)phenyl)methanol; MS 220 m/z (M+1).

Methyl 2-(4-nitro-1H-imidazol-1-yl)-2-phenylacetate; MS 262 m/z (M+1).

The following nitroimidazoles were were prepared by methods analogous to those described above for General Method H:

2,2-dimethyl-N-(2-(4-nitro-1H-imidazol-1-yl)-2-phenylethyl)propan-1-amine

Methyl 2-(4-nitro-1H-imidazol-1-yl)-2-phenylacetate was converted to the title compound using a method analagous to the general procedure H to afford the title compound: MS 303 m/z (M+1).

The following prepared as descripted:

4-Nitro-1-(2-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazole

A mixture of the 2-(4-Nitro-imidazol-1-yl)-cyclobutanecarboxylic acid methyl ester (2.640 g, 0.01105 mol), borane-dimethyl sulfide complex (1M in tetrahydrofuran) (33.2 mL, 0.0332 mol) and tetrahydrofuran (10 mL) was heated at reflux for 17 hours. The reaction was quenched by water. The volatile solvent was evaporated under reduced pressure. The residue was diluted with water and extracted with ethyl acetate three times. The combined extracts were washed with brine and dried over sodium sulfate. The solvent was then evaporated under reduced pressure to yield [2-(4-Nitro-imidazol-1-yl)-cyclobutyl]-methanol (0.825 g, 0.00419 mol) as a white solid. M+1=198.1.

[2-(4-Nitro-imidazol-1-yl)-cyclobutyl]-methanol was converted to Methanesulfonic acid 2-(4-nitro-imidazol-1-yl)-cyclobutylmethyl ester following General Procedure N; MS 276.3 m/z (M+1).

Methanesulfonic acid 2-(4-nitro-imidazol-1-yl)-cyclobutylmethyl ester was converted to the title compound following General Procedure O; MS 251.5 m/z (M+1).

The following mesylates were were prepared by methods analogous to those described above for General Method N:

Methanesulfonic acid 2-{4-[2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-hydroxy-ethyl)-1H-imidazol-4-yl]-amide amide (U.S. Serial No. 11/078,898 filed March 11, 2005) was converted to the title compound; MS 459.0 m/z (M+1).

Methanesulfonic acid 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester

2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(3-hydroxy-propyl)-1H-imidazol-4-yl]-amide was converted to the title compound; MS 485 m/z (M+1).

Methanesulfonic acid 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester

2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(2-hydroxy-1-methyl-ethyl)-1H-imidazol-4-yl]-amide was converted to the title compound; MS 485.5 m/z (M+1).

Methanesulfonic acid 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-3-methyl-butyl ester

2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(3-hydroxy-1,1-dimethyl-propyl)-1H-imidazol-4-yl]-amide was converted to the title compound; MS 513 m/z (M+1).

The following intermediates were prepared by methods analogous to those described above for the reduction of the appropriate nitroimdiazole using General Method G followed by coupling to the appropriate acid using General Procedure A, method F.

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-benzyl-1H-imidazol-4-yl)-amide

1-Benzyl-4-nitro-1H-imidazole was reduced and coupled with 2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid to afford the title compound; MS 470 m/z (M+1).

(4-{2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-acetic acid methyl ester

(4-Nitro-imidazol-1-yl)-acetic acid methyl ester was reduced and coupled with 2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid to afford the title compound; MS 409.1 m/z (M+1).

1-(4-{2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-cyclobutanecarboxylic acid methyl ester

1-(4-Nitro-imidazol-1-yl)-cyclobutanecarboxylic acid methyl ester was reduced and coupled with 2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid to afford the title compound; MS 463.0 m/z (M+1).

2-(4-{2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-cyclobutanecarboxylic acid methyl ester

2-(4-Nitro-imidazol-1-yl)-cyclobutanecarboxylic acid methyl ester was reduced and coupled with 2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid to afford the title compound; MS 463.1 m/z (M+1).

1-{4-[2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-cyclobutanecarboxylic acid methyl ester

1-(4-Nitro-imidazol-1-yl)-cyclobutanecarboxylic acid methyl ester was reduced and coupled with 2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid acid to afford the title compound; MS 475.5 m/z (M+1).

2-{4-[2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-2-methyl-propionic acid methyl ester

2-Methyl-2-(4-nitro-imidazol-1-yl)-propionic acid methyl ester was reduced and coupled with 2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionic acid to afford the title compound; MS 421.5 m/z (M+1).

2-{4-[2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propionic acid methyl ester

2-(4-Nitro-imidazol-1-yl)-propionic acid methyl ester was reduced and coupled with 2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid to afford the title compound; MS 435.5 m/z (M+1).

3-{4-[2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-3-methyl-butyric acid methyl ester

3-Methyl-3-(4-nitro-imidazol-1-yl)-butyric acid methyl ester was reduced and coupled with 2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid to afford the title compound; MS 463.5 m/z (M+1).

2-{4-[2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-2-methyl-propionic acid methyl ester

2-Methyl-2-(4-nitro-imidazol-1-yl)-propionic acid methyl ester was reduced and coupled with 2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid to afford the title compound; MS 449.3 m/z (M+1).

{1-[1-(3-oxo-butyl)-1H-imidazol-4-ylcarbamoyl]-butyl}-carbamic acid tert-butyl ester

4-(4-nitro-1H-imidazol-1-yl)butan-2-one was reduced and coupled with 2-[(tert-butoxycarbonyl)amino]pentanoic acid to afford the title compound; MS 353 m/z (M+1).

3-{4-[2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propionic acid methyl ester; MS 435 m/z (M+1).

2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-methyl-3-oxo-butyl)-1H-imidazol-4-yl]-amide; MS 433 m/z (M+1).

The following Boc groups were removed following general method D;

2-Amino-pentanoic acid [1-(3-oxo-butyl)-1H-imidazol-4-yl]-amide hydrochloride; MS 253 m/z (M+1).

2-Amino-pentanoic acid {1-[2-(2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide; MS 352.3 m/z (M+1).

2-Amino-pentanoic acid (1-{1,1-dimethyl-3-[(pyridin-2-ylmethyl)-amino]-propyl}-1H-imidazol-4-yl)-amide; MS 359 m/z (M+1).

2-Amino-pentanoic acid {1-[1,1-dimethyl-3-(2,2,2-trifluoro-1-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide; MS 426 m/z (M+1).

2-Amino-pentanoic acid {1-[1,1-dimethyl-3-(1-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide; MS 372 m/z (M+1).

The following alcohols were prepared by reduction of the corresponding esters using methods analogous to those described above using General Method I;

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-hydroxy-ethyl)-1H-imidazol-4-yl]-amide; MS 381.1 m/z (M+1).

2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(3-hydroxy-propyl)-1H-imidazol-4-yl]-amide; MS 407m/z (M+1).

2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(2-hydroxy-1-methyl-ethyl)-1H-imidazol-4-yl]-amide; MS 407.5 m/z (M+1).

{1-[1-(3-Hydroxy-1,1-dimethyl-propyl)-1H-imidazol-4-ylcarbamoyl]-butyl}-carbamic acid tert-butyl ester; MS 369 m/z (M+1).

The following aldehydes were prepared by oxidation from corresponding alcohol using methods analogous to those described above using General Method J;

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-formyl-cyclobutyl)-1H-imidazol-4-yl]-amide; MS 419.1 m/z (M+1).

2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-formyl-cyclobutyl)-1H-imidazol-4-yl]-amide; MS 431.5 m/z (M+1).

(2S)-2-(5,7-difluoro-1,2,3,4-tetrahydronaphthalen-3-ylamino)-N-(1-(2-formylphenyl)-1H-imidazol-4-yl)pentanamide;

{1-[1-(1,1-Dimethyl-3-oxo-propyl)-1H-imidazol-4-ylcarbamoyl]-butyl}-carbamic acid tert-butyl ester; MS 367 m/z (M+1).

The following acids were prepared by hydrolysis from corresponding esters using methods analogous to those described above using General Method R;

3-{4-[2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-3-methyl-butyric acid methyl ester; MS 449.6 m/z (M+1).

2-{4-[2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-2-methyl-propionic acid; MS 435.4 m/z (M+1).

2-{4-[2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-2-methyl-propionic acid; MS 407.5 m/z (M+1).

Procedure for Synthesis of 2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid; General procedure Q:

Combine L-norvaline methyl ester-hydrochloride (1 equiv) with 6,8-difluoro-3,4-dihydro-1H-naphthalen-2-one (1 equiv) in methylene chloride and stir 30 min. and add sodium triacetoxy borohydride (1.1 equiv) and stir at rt overnight. The reaction is quenched with aqueous sodium bicarbonate, extracted with methylene chloride, dried, and concentrated. The resultant material is purified by silica gel chromatography to afford the separated diastereomers of 2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid methyl ester: Diastereomer 1; 13C NMR (100 MHz, CDCl3) 14.0, 19.4, 27.7, 28.2, 29.5, 29.6, 36.3, 51.1, 58.7, 100.7, 100.9, 101.2, 110.5, 110.7, 110.8, 118.5, 118.6, 141.1, 159.7, 159.8, 162.1, 176.7; MS m/z 298.3 (M+1). Diastereomer 2; Diagnostic 13C NMR (100 MHz, CDCl3) 14.0, 19.3, 28.3, 28.4, 28.5, 30.3, 36.4, 51.1, 52.0, 58.5, 100.7, 100.9, 101.2, 110.5, 110.7, 176.8; MS m/z 298.3 (M+1).

2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid methyl ester (1 equiv) is dissolved in THF:water (5:1) and LiOH (1.2 equiv) is added. The reaction is stirred overnight at rt, the solvent is removed, water added, and the pH is adjusted to 7 using 1N hydrochloric acid. The solid is filtered, washed with water and diethyl ether, and dried to afford 2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid; Acid derived from diasteromer 1: H1 NMR (400 MHz, CD3OD) 0.99 (t, 3H, J=7.5), 1.48 (m, 2H), 1.82 (m, 3H), 2.36 (m, 1H), 2.65 (m, 1H), 2.95 (m, 2H), 3.28 (s, 1H), 3.42 (m, 1H), 3.74 (m, 1H), 6.80 (m, 2H); (MS m/z 284.3 (M+1). Acid derived from diasteromer 2: H1 NMR (400 MHz, CD3OD) 0.94 (t, 3H, J=7.6), 1.42 (m, 2H), 1.56 (m, 3H), 1.96 (m, 1H), 2.25 (m, 1H), 2.85 (m, 3H), 3.15 (m, 1H), 3.25 (m, 1H), 6.64 (m, 2H); MS m/z 284.2 (M+1).

The following intermdediates were prepared in an analogous manner to Method Q starting with an appropriate amino acid and ketone or starting amino-ester and ketone; or the aminoester is acylated using general procedure A followed by hydrolysis.

(S)-2-(2-(3,5-difluorophenyl)acetamido)-2-phenylacetic acid; MS 304 m/z (M-1).

(S)-2-(2-(3,5-difluorophenyl)acetamido)-2-(pyridin-3-yl)acetic acid; MS 305 m/z (M-1).

(S)-2-(2-(3,5-difluorophenyl)acetamido)-2-(4-fluorophenyl)acetic acid; MS 322 m/z (M-1).

(S)-2-(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-3-ylamino)-2-phenylacetic acid; MS 316 m/z (M-1).

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionic acid; MS 256.5 m/z (M+1).

(S)-2-(1,2,3,4-Tetrahydro-naphthalen-2-ylamino)-pentanoic acid; MS 246.5 m/z (M-1).

The following intermediates were prepared in an analogous manner to Method B starting with an appropriate amine and ketone/aldehyde.

(1-{1-[2-(2,6-Dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-ylcarbamoyl}-butyl)-carbamic acid tert-butyl ester; MS 452.1 m/z (M+1).

2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(3-oxo-butyl)-1H-imidazol-4-yl]-amide; MS 419 m/z (M+1).

[1-(1-{1,1-Dimethyl-3-[(pyridin-2-ylmethyl)-amino]-propyl}-1H-imidazol-4-ylcarbamoyl)-butyl]-carbamic acid tert-butyl ester; MS 459 m/z (M+1).

(1-{1-[1,1-Dimethyl-3-(2,2,2-trifluoro-1-phenyl-ethylamino)-propyl]-1H-imidazol-4-ylcarbamoyl}-butyl)-carbamic acid tert-butyl ester; MS 526 m/z (M+1).

(1-{1-[1,1-Dimethyl-3-(1-phenyl-ethylamino)-propyl]-1H-imidazol-4-ylcarbamoyl}-butyl)-carbamic acid tert-butyl ester; MS 472 m/z (M+1).

The following Examples were prepared by methods analogous to those described above for General Procedure O;

Example 1

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-ethoxy-propylamino)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with 3-ethoxypropyl amine to provide the title compound: MS 446.2 m/z (M+1).

Example 2

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(octahydro-pyrazino[1,2-a]azepin-2-yl)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 517.2 m/z (M+1);.

Example 3

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-([1,4]dioxan-2-ylmethyl-methyl-amino)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 494.2 m/z (M+1).

Example 4

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(2-methoxy-1-methyl-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 452.2 m/z (M+1).

Example 5

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-oxo-piperazin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 463.2 m/z (M+1).

Example 6

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-benzylamino-ethyl)-1H-imidazol-4-yl]-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 470.2 m/z (M+1).

Example 7

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-butoxy-propylamino)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 494.2 m/z (M+1).

Example 8

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-((1R,2S)-2-hydroxymethyl-cyclohexylamino)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 492.2 m/z (M+1).

Example 9

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[(4aS,8aS)-2-(octahydro-isoquinolin-2-yl)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 502.2 m/z (M+1).

Example 10

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-isopropoxy-propylamino)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 480.2 m/z (M+1).

Example 11

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(octahydro-isoquinolin-2-yl)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 502.2 m/z (M+1).

Example 12

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3,4,5,6-tetrahydro-2H-[4,4']bipyridinyl-1-yl)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 525.2 m/z (M+1).

Example 13

S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(2-hydroxy-2-phenyl-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 500.2 m/z (M+1).

Example 14

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(indan-1-ylamino)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 496.2 m/z (M+1).

Example 15

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(benzyl-methyl-amino)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 484.2 m/z (M+1).

Example 16

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(indan-2-ylamino)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 496.2 m/z (M+1).

Examle 17

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3,4-dihydro-1#H!-isoquinolin-2-yl)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 496.2 m/z (M+1).

Example 18

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(2-propoxy-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 466.2 m/z (M+1).

Example 19

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-benzyl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 524.2 m/z (M+1).

Example 20

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-pyridin-2-yl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 511.2 m/z (M+1).

Example 21

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(methyl-pyridin-4-ylmethyl-amino)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 485.2 m/z (M+1).

Example 22

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{2-[(2-methanesulfonyl-ethyl)-methyl-amino]-ethyl}-1H-imidazol-4-yl)-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 500.1 m/z (M+1).

Example 23

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(2-tert-butoxy-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 480.2 m/z (M+1).

Example 23A

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-pyridin-4-yl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-(4-{2-[2-(3,5-difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-ethyl ester was reacted with appropriate amine to provide the title compound: MS 511.2 m/z (M+1).

The following Examples were prepared by methods analogous to those described above for General Procedure P;

Example 24

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-fluoro-benzyl)-1H-imidazol-4-yl]-amide

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1H-imidazol-4-yl)-amide was reacted with appropriate benzyl halide to provide the title compound: MS 445.1 m/z (M+1).

Example 25

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(3-fluoro-benzyl)-1H-imidazol-4-yl]-amide

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1H-imidazol-4-yl)-amide was reacted with appropriate benzyl halide to provide the title compound: MS 445.1 m/z (M+1.

Example 26

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(4-methyl-benzyl)-1H-imidazol-4-yl]-amide

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1H-imidazol-4-yl)-amide was reacted with appropriate benzyl halide to provide the title compound: MS 441.1 m/z (M+1).

Example 27

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(4-methoxy-benzyl)-1H-imidazol-4-yl]-amide

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1H-imidazol-4-yl)-amide was reacted with appropriate benzyl halide to provide the title compound: MS 457.3 m/z (M+1).

Example 28

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(4-tert-butyl-benzyl)-1H-imidazol-4-yl]-amide

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1H-imidazol-4-yl)-amide was reacted with appropriate benzyl halide to provide the title compound: MS 483.3 m/z (M+1).

The following Examples were prepared by methods analogous to those described above for General Procedure B;

Example 29

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-formyl-cyclobutyl)-1H-imidazol-4-yl]-amide was reacted with appropriate amine to provide the title compound: MS 474.1 m/z (M+1).

Example 30

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-dimethylaminomethyl-cyclobutyl)-1H-imidazol-4-yl]-amide

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-formyl-cyclobutyl)-1H-imidazol-4-yl]-amide was reacted with appropriate amine to provide the title compound: MS 448.5 m/z (M+1).

Example 31

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-piperidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-formyl-cyclobutyl)-1H-imidazol-4-yl]-amide was reacted with appropriate amine to provide the title compound: MS 488.5 m/z (M+1).

Example 32

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-morpholin-4-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-formyl-cyclobutyl)-1H-imidazol-4-yl]-amide was reacted with appropriate amine to provide the title compound: MS 490.5 m/z (M+1).

Example 31A

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1-[((2R,6S)-2,6-dimethyl-morpholin-4-yl)methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-formyl-cyclobutyl)-1H-imidazol-4-yl]-amide was reacted with appropriate amine to provide the title compound: MS 518.5 m/z (M+1).

Example 32A

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1-[(2,2,2-trifluoro-ethylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-formyl-cyclobutyl)-1H-imidazol-4-yl]-amide was reacted with appropriate amine to provide the title compound: MS 502.4 m/z (M+1).

Example 33

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1-[((R)-1-cyclohexyl-ethylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-formyl-cyclobutyl)-1H-imidazol-4-yl]-amide was reacted with appropriate amine to provide the title compound: MS 530.5 m/z (M+1).

Example 34

(S)-2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide

2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-formyl-cyclobutyl)-1H-imidazol-4-yl]-amide was reacted with appropriate amine to provide the title compound: MS 486.5 m/z (M+1).

Example 35

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1-[(2,2-dimethyl-propylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-formyl-cyclobutyl)-1H-imidazol-4-yl]-amide was reacted with appropriate amine to provide the title compound: MS 490.5 m/z (M+1).

Example 36

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(2,2,2-trifluoro-ethylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide

2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-formyl-cyclobutyl)-1H-imidazol-4-yl]-amide was reacted with appropriate amine to provide the title compound: MS 514.5 m/z (M+1).

Example 37

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(2,2-dimethyl-propylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide

2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-formyl-cyclobutyl)-1H-imidazol-4-yl]-amide was reacted with appropriate amine to provide the title compound: MS 502.6 m/z (M+1).

Example 38

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[((R)-1-cyclohexyl-ethylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide

2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-formyl-cyclobutyl)-1H-imidazol-4-yl]-amide was reacted with appropriate amine to provide the title compound: MS 542.6 m/z (M+1).

Example 39

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-dimethylaminomethyl-cyclobutyl)-1H-imidazol-4-yl]-amide

2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-formyl-cyclobutyl)-1H-imidazol-4-yl]-amide was reacted with appropriate amine to provide the title compound: MS 460.6 m/z (M+1).

Example 40

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-piperidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide

2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-formyl-cyclobutyl)-1H-imidazol-4-yl]-amide was reacted with appropriate amine to provide the title compound: MS 500.6 m/z (M+1).

Example 41

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-morpholin-4-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide

2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-formyl-cyclobutyl)-1H-imidazol-4-yl]-amide was reacted with appropriate amine to provide the title compound: MS 502.6 m/z (M+1).

Example 42

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[((2R,6S)-2,6-dimethyl-morpholin-4-yl)methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide

2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-formyl-cyclobutyl)-1H-imidazol-4-yl]-amide was reacted with appropriate amine to provide the title compound: MS 530.6 m/z (M+1).

Example 43

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-((R)-1-cyclohexyl-ethylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide

2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1,1-dimethyl-2-oxo-ethyl)-1H-imidazol-4-yl]-amide (U.S. Serial No. 11/078,898 filed March 11, 2005) was treated with the appropriate amine to afford the title compound MS 530.4 m/z (M+1).

Example 44

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1,1-dimethyl-2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide

2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1,1-dimethyl-2-oxo-ethyl)-1H-imidazol-4-yl]-amide (U.S. Serial No. 11/078,898 filed March 11, 2005) was treated with the appropriate amine to afford the title compound MS 518.4 m/z (M+1).

Example 45

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(1-hydroxy-cyclohexylmethyl)-amino]-1,1-dimethyl-ethyl}-1H-imidazol-4-yl)-amide

2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1,1-dimethyl-2-oxo-ethyl)-1H-imidazol-4-yl]-amide (U.S. Serial No. 11/078,898 filed March 11, 2005) was treated with the appropriate amine to afford the title compound MS 532.6 m/z (M+1).

Example 46

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(4-hydroxy-tetrahydro-pyran-4-ylmethyl)-amino]-1,1-dimethyl-ethyl}-1H-imidazol-4-yl)-amide

2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1,1-dimethyl-2-oxo-ethyl)-1H-imidazol-4-yl]-amide (U.S. Serial No. 11/078,898 filed March 11, 2005) was treated with the appropriate amine to afford the title compound MS 534.6 m/z (M+1).

Example 47

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(2-methoxy-2-methyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide

2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1,1-dimethyl-2-oxo-ethyl)-1H-imidazol-4-yl]-amide (U.S. Serial No. 11/078,898 filed March 11, 2005) was treated with the appropriate amine to afford the title compound MS 506.5 m/z (M+1).

Example 48

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1,1-dimethyl-2-[(3-methyl-oxetan-3-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide

2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1,1-dimethyl-2-oxo-ethyl)-1H-imidazol-4-yl]-amide (U.S. Serial No. 11/078,898 filed March 11, 2005) was treated with the appropriate amine to afford the title compound MS 504.5 m/z (M+1).

Example 49

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(cyclohexylmethyl-amino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide

2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1,1-dimethyl-2-oxo-ethyl)-1H-imidazol-4-yl]-amide (U.S. Serial No. 11/078,898 filed March 11, 2005) was treated with the appropriate amine to afford the title compound MS 516.6 m/z (M+1).

Example 50

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-((R)-1-cyclohexyl-ethylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1,1-dimethyl-2-oxo-ethyl)-1H-imidazol-4-yl]-amide (U.S. Serial No. 11/078,898 filed March 11, 2005) was treated with the appropriate amine to afford the title compound MS 518.2 m/z (M+1).

Example 51

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1,1-dimethyl-2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1,1-dimethyl-2-oxo-ethyl)-1H-imidazol-4-yl]-amide (U.S. Serial No. 11/078,898 filed March 11, 2005) was treated with the appropriate amine to afford the title compound MS 506.4 m/z (M+1).

Example 52

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-((S)-1-phenyl-ethylamino)-butyl]-1H-imidazol-4-yl}-amide

2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(3-oxo-butyl)-1H-imidazol-4-yl]-amide was treated with the appropriate amine to afford the title compound MS 524.1 m/z (M+1).

Example 53

(S)-2-(Dicyclopropylmethyl-amino)-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide

2-Amino-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide (U.S. Serial No. 11/078,898 filed March 11, 2005) was treated with the appropriate ketone to afford the title compound MS 402.6 m/z (M+1).

The following Examples were prepared by methods analogous to those described above for General Procedure I;

Example 54

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-hydroxymethyl-cyclobutyl)-1H-imidazol-4-yl]-amide

1-(4-{2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-cyclobutanecarboxylic acid methyl ester was reduced to afford the title compound: MS 421.1 m/z (M+1).

Example 55

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-hydroxymethyl-cyclobutyl)-1H-imidazol-4-yl]-amide

2-(4-{2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoylamino}-imidazol-1-yl)-cyclobutanecarboxylic acid methyl ester was reduced to afford the title compound: MS 421.1 m/z (M+1).

Example 56

(S)-2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-hydroxymethyl-cyclobutyl)-1H-imidazol-4-yl]-amide

1-{4-[2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-cyclobutanecarboxylic acid methyl ester was reduced to afford the title compound: MS 433.5 m/z (M+1).

The following Examples were prepared by methods analogous to those described above for General Procedure K;

Example 57

(S)-2-[2-(2,4-Difluoro-phenyl)-2-hydroxy-ethylamino]-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide

2-Amino-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide (U.S. Serial No. 11/078,898 filed March 11, 2005) was treated with the appropriate epoxide to afford the title compound: MS 464.3 m/z (M+1).

Example 58

(S)-2-[2-(3,4-Difluoro-phenyl)-2-hydroxy-ethylamino]-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide

2-Amino-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide (U.S. Serial No. 11/078,898 filed March 11, 2005) was treated with the appropriate epoxide to afford the title compound: MS 464.3 m/z (M+1).

Example 59

(S)-2-[2-(3,5-Difluoro-phenyl)-2-hydroxy-ethylamino]-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide

2-Amino-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide (U.S. Serial No. 11/078,898 filed March 11, 2005) was treated with the appropriate epoxide to afford the title compound: MS 464.5 m/z (M+1).

Example 60

(S)-2-[2-(2,4-Difluoro-phenyl)-2-hydroxy-ethylamino]-pentanoic acid {1-[2-((2R,6S)-2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide

2-Amino-pentanoic acid [1-(1,1-dimethyl-2-(2,6-dimethylmorpholino-1-yl-ethyl)-1H-imidazol-4-yl]-amide was treated with the appropriate epoxide to afford the title compound: MS 508.5 m/z (M+1).

Example 61

(S)-2-[(1-Hydroxy-cyclohexylmethyl)-amino]-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide

2-Amino-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide (U.S. Serial No. 11/078,898 filed March 11, 2005) was treated with the appropriate epoxide to afford the title compound: MS 420.6 m/z (M+1).

The following Examples were prepared by methods analogous to those described above for General Procedure O;

Example 62

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-((R)-1-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester was treated with the appropriate amine to afford the title compound: MS 510.1 m/z (M+1).

Example 63

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(3-methyl-benzylamino)-propyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester was treated with the appropriate amine to afford the title compound: MS 510.53 m/z (M+1).

Example 64

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(2-hydroxy-2-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester was treated with the appropriate amine to afford the title compound: MS 526.54 m/z (M+1).

Example 65

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(2-chloro-benzylamino)-propyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester was treated with the appropriate amine to afford the title compound: MS 530.5 m/z (M+1).

Examle 66

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(3,4-dihydro-1H-isoquinolin-2-yl)-propyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester was treated with the appropriate amine to afford the title compound: MS 522.53 m/z (M+1).

Example 67

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(indan-2-ylamino)-propyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester was treated with the appropriate amine to afford the title compound: MS 522.52 m/z (M+1).

Example 68

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(1-methoxymethyl-propylamino)-propyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester was treated with the appropriate amine to afford the title compound: MS 492.53 m/z (M+1).

Example 69

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(4-chloro-benzylamino)-propyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester was treated with the appropriate amine to afford the title compound: MS 530.5 m/z (M+1).

Example 70

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(2-methyl-benzylamino)-propyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester was treated with the appropriate amine to afford the title compound: MS 510.5 m/z (M+1).

Example 71

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(2-methoxy-ethylamino)-propyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester was treated with the appropriate amine to afford the title compound: MS 464.2 m/z (M+1).

Example 72

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{3-[(pyridin-3-ylmethyl)-amino]-propyl}-1H-imidazol-4-yl)-amide

Methanesulfonic acid 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester was treated with the appropriate amine to afford the title compound: MS 497.5 m/z (M+1).

Example 73

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-((S)-1-p-tolyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester was treated with the appropriate amine to afford the title compound: MS 524.6 m/z (M+1).

Example 74

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(4-methoxy-benzylamino)-propyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester was treated with the appropriate amine to afford the title compound: MS 526.5m/z (M+1).

Example 75

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(cyclopropylmethyl-amino)-propyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester was treated with the appropriate amine to afford the title compound: MS 460.5 m/z (M+1).

Example 76

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(4-methyl-benzylamino)-propyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester was treated with the appropriate amine to afford the title compound: MS 510.5 m/z (M+1).

The following Examples were prepared by methods analogous to those described above for General Procedure A, method F using 2-{4-[2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-2-methyl-propionic acid and an appropriate amine.

Example 77

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-methyl-1-(methyl-phenethyl-carbamoyl)-ethyl]-1H-imidazol-4-yl}-amide

MS 552.58 m/z (M+1).

Example 78

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(1,3-dihydro-isobenzofuran-5-ylcarbamoyl)-1-methyl-ethyl]-1H-imidazol-4-yl}-amide

MS 552.55 m/z (M+1).

Example 79

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(indan-1-ylcarbamoyl)-1-methyl-ethyl]-1H-imidazol-4-yl}-amide

MS 550.53 m/z (M+1).

Example 80

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-2-oxo-2-(3-pyridin-4-yl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide

MS 565.6 m/z (M+1).

Example 81

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[2-(3-fluoro-phenyl)-ethylcarbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide

MS 556.54 m/z (M+1).

Example 82

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(3-cyano-piperidin-1-yl)-1,1-dimethyl-2-oxo-ethyl]-1H-imidazol-4-yl}-amide

MS 527.57 m/z (M+1).

Example 83

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[methyl-(tetrahydro-pyran-2-ylmethyl)-carbamoyl]-ethyl}-1H-imidazol-4-yl)-amide

MS 546.58 m/z (M+1).

Example 84

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[ethyl-(2-pyrazol-1-yl-ethyl)-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide

MS 556.61m/z (M+1).

Example 85

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-2-oxo-2-(2-phenyl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide

MS 564.59 m/z (M+1).

Example 86

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(furan-2-ylmethyl)-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide

MS 514.51m/z (M+1).

Example 87

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[3-(acetyl-methyl-amino)-pyrrolidin-1-yl]-1,1-dimethyl-2-oxo-ethyl}-1H-imidazol-4-yl)-amide

MS 559.57 m/z (M+1).

Example 88

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-methyl-1-((3R,4S)-4-methylsulfanyl-tetrahydro-furan-3-ylcarbamoyl)-ethyl]-1H-imidazol-4-yl}-amide

MS 550.53 m/z (M+1).

Example 89

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(4-acetyl-[1,4]diazepan-1-yl)-1,1-dimethyl-2-oxo-ethyl]-1H-imidazol-4-yl}-amide

MS 559.31 m/z (M+1).

Example 90

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[1-(1-methyl-1H-pyrazol-4-yl)-ethylcarbamoyl]-ethyl}-1H-imidazol-4-yl)-amide

MS 542.56 m/z (M+1). .

Example 91

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(3-methoxy-propylcarbamoyl)-1-methyl-ethyl]-1H-imidazol-4-yl}-amide

MS 506.52 m/z (M+1).

Example 92

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[(3-methyl-[1,2,4]oxadiazol-5-ylmethyl)-carbamoyl]-ethyl}-1H-imidazol-4-yl)-amide

MS 530.54 m/z (M+1).

Example 93

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(2-cyano-ethyl)-methyl-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide

MS 501.51 m/z (M+1).

Example 94

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-2-(3-methyl-5,6-dihydro-8H-[1,2,4]triazolo[4,3-a]pyrazin-7-yl)-2-oxo-ethyl]-1H-imidazol-4-yl}-amide

MS 555.55 m/z (M+1).

Example 95

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[methyl-(1-methyl-1H-imidazol-2-ylmethyl)-carbamoyl]-ethyl}-1H-imidazol-4-yl)-amide

MS 542.48 m/z (M+1).

Example 96

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(2-diethylamino-ethyl)-methyl-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide

MS 547.62 m/z (M+1).

The following Examples were prepared by methods analogous to those described above for General Procedure A, method F using 2-{4-[2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-2-methyl-propionic acid and an appropriate amine.

Example 97

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-indan-1-yl-isobutyramide

MS 522.56 m/z (M+1).

Example 98

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[1,1-dimethyl-2-oxo-2-(3-pyridin-4-yl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-propionamide

MS 537.53 m/z (M+1).

Example 99

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[2-(4-hydroxymethyl-4-methyl-piperidin-1-yl)-1,1-dimethyl-2-oxo-ethyl]-1H-imidazol-4-yl}-propionamide

MS 528.51 m/z (M+1).

Example 100

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-methyl-N-phenethyl-isobutyramide

MS 524.54 m/z (M+1).

Example 101

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-ethyl-N-(2-pyrazol-1-yl-ethyl)-isobutyramide

MS 528.49 m/z (M+1).

Example 102

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[2-(4-hydroxymethyl-4-methyl-piperidin-1-yl)-1,1-dimethyl-2-oxo-ethyl]-1H-imidazol-4-yl}-propionamide

MS 518.53 m/z (M+1).

Example 103

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(4-methyl-benzyl)-isobutyramide

MS 510.49 m/z (M+1).

Example 104

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(1,3-dihydro-isobenzofuran-5-yl)-isobutyramide

MS 524.47 m/z (M+1).

Example 105

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[1,1-dimethyl-2-oxo-2-(2-phenyl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-propionamide

MS 536.55 m/z (M+1).

Example 106

(S)-N-{1-[2-(3-Cyano-piperidin-1-yl)-1,1-dimethyl-2-oxo-ethyl]-1H-imidazol-4-yl}-2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionamide

MS 499.46 m/z (M+1).

Example 107

(S)-N-(1-{2-[3-(Acetyl-methyl-amino)-pyrrolidin-1-yl]-1,1-dimethyl-2-oxo-ethyl}-1H-imidazol-4-yl)-2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionamide

MS 531.53 m/z (M+1).

Example 108

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-((1R,2S)-2-hydroxymethyl-cyclohexyl)-isobutyramide

MS 518.53 m/z (M+1).

Example 109

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(3-methyl-[1,2,4]oxadiazol-5-ylmethyl)-isobutyramide

MS 502.43 m/z (M+1).

Example 110

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-((S)-2-methoxy-1-methyl-ethyl)-isobutyramide

MS 478.51 m/z (M+1).

Example 111

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(3-methoxy-propyl)-isobutyramide

MS 478.58 m/z (M+1).

Example 112

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-[1-(1-methyl-1H-pyrazol-4-yl)-ethyl]-isobutyramide

MS 514.51 m/z (M+1).

Example 113

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(3-imidazol-1-yl-propyl)-isobutyramide

MS 514.56 m/z (M+1).

Example 114

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(3-morpholin-4-yl-propyl)-isobutyramide

MS 533.58 m/z (M+1).

The following Examples were prepared by methods analogous to those described above for the reduction of the appropriate nitroimdiazole using General Method G followed by coupling to the appropriate acid using General Procedure A, method F.

Example 115

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(3-methyl-oxetan-3-ylmethyl)-1H-imidazol-4-yl]-amide

1-(3-Methyl-oxetan-3-ylmethyl)-4-nitro-1H-imidazole was reduced and then coupled with 2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (U.S. Serial No. 11/078,898 filed March 11, 2005) to afford the title compound: MS 433.3 m/z (M+1).

Example 116

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(3-methyl-oxetan-3-ylmethyl)-1H-imidazol-4-yl]-amide

1-(3-Methyl-oxetan-3-ylmethyl)-4-nitro-1H-imidazole was reduced and then coupled with 2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (U.S. Serial No. 11/078,898 filed March 11, 2005) to afford the title compound: MS 421.3 m/z (M+1).

Example 117

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(4-trifluoromethyl-phenyl)-ethyl]-1H-imidazol-4-yl}-amide

4-Nitro-1-[1-(4-trifluoromethyl-phenyl)-ethyl]-1H-imidazole was reduced and then coupled with 2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (U.S. Serial No. 11/078,898 filed March 11, 2005) to afford the title compound: MS 521.5 m/z (M+1).

Example 118

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[1-(4-trifluoromethyl-phenyl)-ethyl]-1H-imidazol-4-yl}-amide

4-Nitro-1-[1-(4-trifluoromethyl-phenyl)-ethyl]-1H-imidazole was reduced and then coupled with with 2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (U.S. Serial No. 11/078,898 filed March 11, 2005) to afford the title compound: MS 509.5 m/z (M+1).

Example 120

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide

4-Nitro-1-(2-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazole was reduced and then coupled with with 2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (U.S. Serial No. 11/078,898 filed March 11, 2005) to afford the title compound: MS 474.6 m/z (M+1).

Example 121

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(2-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide

4-Nitro-1-(2-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazole was reduced and then coupled with 2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (U.S. Serial No. 11/078,898 filed March 11, 2005) to afford the title compound: MS 486.6 m/z (M+1).

Example 122

(S)-2-(1,2,3,4-Tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1,1-dimethyl-2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide

[2-(4-Nitro-imidazol-1-yl)-propyl]-(tetrahydro-pyran-4-ylmethyl)-amine was reduced and then coupled with 2-(1,2,3,4-Tetrahydro-naphthalen-2-ylamino)-pentanoic acid to afford the title compound: MS 482.6 m/z (M+1).

Example 123

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(2-ethoxy-ethylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide

(2-Ethoxy-ethyl)-[2-methyl-2-(4-nitro-imidazol-1-yl)-propyl]-amine was reduced and then coupled with 2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (U.S. Serial No. 11/078,898 filed March 11, 2005) to afford the title compound: MS 492.6 m/z (M+1).

Example 124

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[2-(2-ethoxy-ethylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-propionamide

(2-Ethoxy-ethyl)-[2-methyl-2-(4-nitro-imidazol-1-yl)-propyl]-amine was reduced and then coupled with 2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionic acid to afford the title compound: MS 464.6 m/z (M+1).

The following Examples were prepared by methods analogous to those described above for General Procedure A, method F

Example 125

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(1-hydroxy-cyclohexylmethyl)-carbamoyl]-1,1-dimethyl-ethyl}-1H-imidazol-4-yl)-amide

3-{4-[2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-3-methyl-butyric acid was coupled with the appropriate amine to afford the title compound: MS 560.5 m/z (M+1).

Example 126

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(1-hydroxy-cyclohexylmethyl)-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide

2-{4-[2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-2-methyl-propionic acid was coupled with the appropriate amine to afford the title compound: MS 546.6 m/z (M+1).

Example 127

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[(tetrahydro-pyran-4-ylmethyl)-carbamoyl]-ethyl}-1H-imidazol-4-yl)-amide

2-{4-[2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-2-methyl-propionic acid was coupled with the appropriate amine to afford the title compound: MS 532.6 m/z (M+1).

Example 128

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-methyl-1-(2-methyl-benzylcarbamoyl)-ethyl]-1H-imidazol-4-yl}-amide

2-{4-[2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-2-methyl-propionic acid was coupled with the appropriate amine to afford the title compound: MS 538.52 m/z (M+1).

Example 129

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(2-methoxy-1-methyl-ethylcarbamoyl)-1-methyl-ethyl]-1H-imidazol-4-yl}-amide

2-{4-[2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-2-methyl-propionic acid was coupled with the appropriate amine to afford the title compound: MS 505.9 m/z (M+1).

The following Examples were prepared by methods analogous to those described above for General Procedure O;

Example 129a

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide

Methanesulfonic acid 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester was reacted with appropriate amine to afford the title compound: MS 504.6 m/z (M+1); The diastereomers were separated using Chiral HPLC conditions (OD-H column (2.1 X 250 cm); 10 mL/min; 95/5 Heptane/EtOH + 0.2% DEA)

Example 130

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(1-hydroxy-cyclohexylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide

Methanesulfonic acid 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-ethyl ester was reacted with the appropriate amine to afford the title: MS 504.6 m/z (M+1).

Example 131

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(4-hydroxy-tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide

Methanesulfonic acid 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-ethyl ester was reacted with the appropriate amine to afford the title: MS 506.6 m/z (M+1).

Example 132

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide

Methanesulfonic acid 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-ethyl ester was reacted with the appropriate amine to afford the title: 490.5 m/z (M+1).

Example 133

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(3-methyl-oxetan-3-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide

Methanesulfonic acid 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-ethyl ester was reacted with the appropriate amine to afford the title: 476.6 m/z (M+1).

Example 133A

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(1-hydroxy-cyclohexylmethyl)-amino]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide

Methanesulfonic acid 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester was reacted with the appropriate amine to afford the title: 518.3 m/z (M+1).

Example 134

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(2-ethoxy-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide

Methanesulfonic acid 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-ethyl ester was reacted with the appropriate amine to afford the title: 464.6 m/z (M+1).

Example 135

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(3-benzylamino-propyl)-1H-imidazol-4-yl]-amide

Methanesulfonic acid 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoylamino]-imidazol-1-yl}-propyl ester was reacted with the appropriate amine to afford the title: 496.3 m/z (M+1);

The following Examples were prepared by methods analogous to those described above for General Procedure B;

Example 136

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1,1-dimethyl-3-[(pyridin-2-ylmethyl)-amino]-propyl}-1H-imidazol-4-yl)-amide

2-Amino-pentanoic acid (1-{1,1-dimethyl-3-[(pyridin-2-ylmethyl)-amino]-propyl}-1H-imidazol-4-yl)-amide was reacted with 6,8-Difluoro-3,4-dihydro-1H-naphthalen-2-one to afford the title: 525.5 m/z (M+1).

Example 137

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-3-((S)-2,2,2-trifluoro-1-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide

2-Amino-pentanoic acid {1-[1,1-dimethyl-3-(2,2,2-trifluoro-1-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide 6,8-Difluoro-3,4-dihydro-1H-naphthalen-2-one to afford the title: 592.3 m/z (M+1).

Example 138

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-3-((R)-1-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide

2-Amino-pentanoic acid {1-[1,1-dimethyl-3-(1-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide was reacted with 6,8-Difluoro-3,4-dihydro-1H-naphthalen-2-one to afford the title: 538.6 m/z (M+1).

Examle 139

(S)-2-(2-Trifluoromethyl-benzylamino)-pentanoic acid {1-[2-((2R,6S)-2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide

2-Amino-pentanoic acid {1-[2-(2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide was reacted with the appropriate aldehyde to afford the title compound: 510.5 m/z (M+1).

Example 140

(S)-2-{[(2-Fluoro-3-trifluoromethyl-phenyl)methyl]-amino}-pentanoic acid {1-[2-((2R,6S)-2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide

2-Amino-pentanoic acid {1-[2-(2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide was reacted with the appropriate aldehyde to afford the title compound: 528.6 m/z (M+1).

The following Examples were prepared by methods analogous to those described above for the reduction of the appropriate nitroimdiazole using General Method G followed by coupling to the appropriate acid using General Procedure A, method F.

Example 140a

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-[1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-2-phenyl-acetamide

1-(2-methyl-1-(pyrrolidin-1-yl)propan-2-yl)-4-nitro-1H-imidazole (U.S. Serial No. 11/078,898 filed March 11, 2005) was reduced and coupled with (S)-2-(2-(3,5-difluorophenyl)acetamido)-2-phenylacetic acid to afford the title compound: MS 496 m/z (M+1).

Example 141

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-{1-[2-((2S,6R)-2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-phenyl-acetamide

2,6-Dimethyl-4-[2-methyl-2-(4-nitro-imidazol-1-yl)-propyl]-morpholine (U.S. Serial No. 11/078,898 filed March 11, 2005) was reduced and coupled with (S)-2-(2-(3,5-difluorophenyl)acetamido)-2-phenylacetic acid to afford the title compound: MS 540 m/z (M+1).

Example 142

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[2-(2,2-dimethyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-phenyl-acetamide

2-methyl-N-neopentyl-2-(4-nitro-1H-imidazol-1-yl)propan-1-amine (U.S. Serial No. 11/078,898 filed March 11, 2005) was reduced and coupled with (S)-2-(5,7-difluoro-1,2,3,4-tetrahydronaphthalen-3-ylamino)-2-phenylacetic acid to afford the title compound: MS 524 m/z (M+1).

Example 143

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-indan-1-yl-1H-imidazol-4-yl)-amide

1-(2,3-dihydro-1H-inden-1-yl)-4-nitro-1H-imidazole was reduced and coupled with (S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (U.S. Serial No. 11/078,898 filed March 11, 2005) to afford the title compound: MS 453 m/z (M+1).

Example 144

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [(S)-1-((1S,2R)-2-hydroxy-indan-1-yl)-1H-imidazol-4-yl]-amide

(1S,2R)-2,3-dihydro-1-(4-nitro-1H-imidazol-1-yl)-1H-inden-2-ol was reduced and coupled with (S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (U.S. Serial No. 11/078,898 filed March 11, 2005) to afford the title compound: MS 469 m/z (M+1).

Example 145

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [(R)-1-((1R,2S)-2-hydroxy-indan-1-yl)-1H-imidazol-4-yl]-amide

(1R,2S)-2,3-dihydro-1-(4-nitro-1H-imidazol-1-yl)-1H-inden-2-ol was reduced and coupled with (S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (U.S. Serial No. 11/078,898 filed March 11, 2005) to afford the title compound: MS 469 m/z (M+1).

Example 146

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[1-(4-fluoro-phenyl)-2-hydroxy-ethyl]-1H-imidazol-4-yl}-amide

2-(4-amino-1H-imidazol-1-yl)-2-(4-fluorophenyl)ethanol was reduced and coupled with (S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (U.S. Serial No. 11/078,898 filed March 11, 2005) to afford the title compound: MS 475 m/z (M+1).

Example 147

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {(R)-1-[(R)-1-(4-fluoro-phenyl)-2-hydroxy-ethyl]-1H-imidazol-4-yl}-amide

(R)-2-(4-amino-1H-imidazol-1-yl)-2-(4-fluorophenyl)ethanol was reduced and coupled with (S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (U.S. Serial No. 11/078,898 filed March 11, 2005) to afford the title compound: MS 475 m/z (M+1).

Example 148

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-hydroxymethyl-phenyl)-1H-imidazol-4-yl]-amide

(2-(4-nitro-1H-imidazol-1-yl)phenyl)methanol was reduced and coupled with (S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (U.S. Serial No. 11/078,898 filed March 11, 2005) to afford the title compound: MS 443 m/z (M+1).

Example 149

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-{1-[2-(2,2-dimethyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-phenyl-acetamide

2-methyl-N-neopentyl-2-(4-nitro-1H-imidazol-1-yl)propan-1-amine (U.S. Serial No. 11/078,898 filed March 11, 2005) was reduced and coupled with (S)-2-(2-(3,5-difluorophenyl)acetamido)-2-phenylacetic acid to afford the title compound: MS 512 m/z (M+1).

Example 150

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {(S)-1-[2-(2,2-dimethyl-propylamino)-1-phenyl-ethyl]-1H-imidazol-4-yl}-amide

(S)-2,2-dimethyl-N-(2-(4-nitro-1H-imidazol-1-yl)-2-phenylethyl)propan-1-amine was reduced and coupled with (S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (U.S. Serial No. 11/078,898 filed March 11, 2005) to afford the title compound: MS 538 m/z (M+1).

Example 151

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {(S)-1-[2-(2,2-dimethyl-propylamino)-1-phenyl-ethyl]-1H-imidazol-4-yl}-amide

(R)-2,2-dimethyl-N-(2-(4-nitro-1H-imidazol-1-yl)-2-phenylethyl)propan-1-amine was reduced and coupled with (S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (U.S. Serial No. 11/078,898 filed March 11, 2005) to afford the title compound: MS 538 m/z (M+1).

Example 152

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-{1-[2-(2,2-dimethyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-(4-fluoro-phenyl)-acetamide

2-methyl-N-neopentyl-2-(4-nitro-1H-imidazol-1-yl)propan-1-amine (U.S. Serial No. 11/078,898 filed March 11, 2005) was reduced and coupled with (S)-2-(2-(3,5-difluorophenyl)acetamido)-2-(4-fluorophenyl)acetic acid to afford the title compound: MS 530 m/z (M+1).

Example 153

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-{1-[2-(2,2-dimethyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-pyridin-3-yl-acetamide

2-methyl-N-neopentyl-2-(4-nitro-1H-imidazol-1-yl)propan-1-amine (U.S. Serial No. 11/078,898 filed March 11, 2005) was reduced and coupled with (S)-2-(2-(3,5-difluorophenyl)acetamido)-2-(pyridin-3-yl)acetic acid to afford the title compound: MS 513 m/z (M+1).

The following Examples were prepared by methods analogous to those described using General Method B

Example 154

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(2,2-dimethyl-propylamino)-methyl]-phenyl}-1H-imidazol-4-yl)-amide

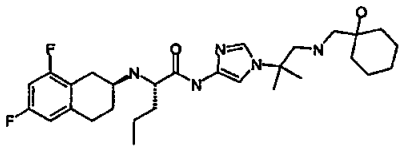
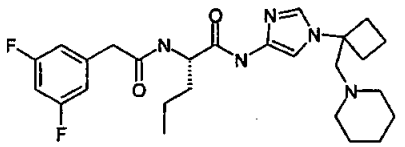
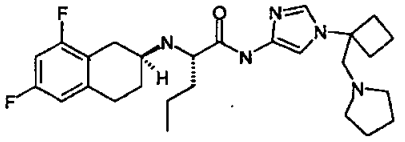
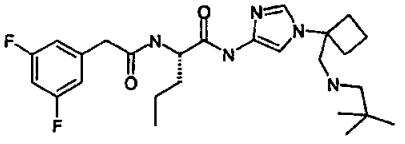
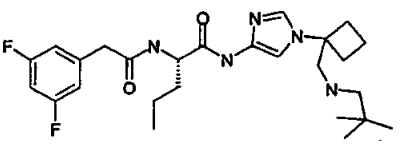
(2S)-2-(5,7-difluoro-1,2,3,4-tetrahydronaphthalen-3-ylamino)-N-(1-(2-formylphenyl)-1H-imidazol-4-yl)pentanamide was treated with the appropriate amine to afford the title compound: MS 524 m/z (M+1).

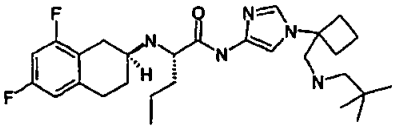
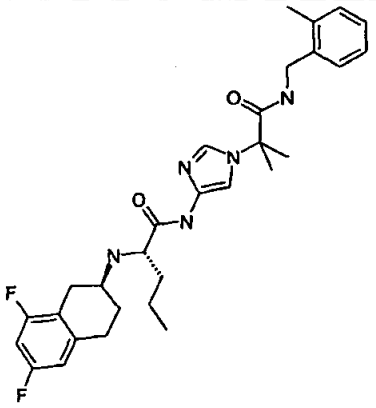
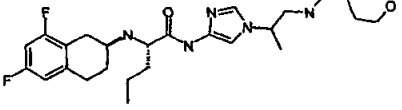
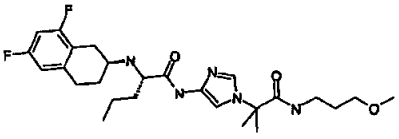
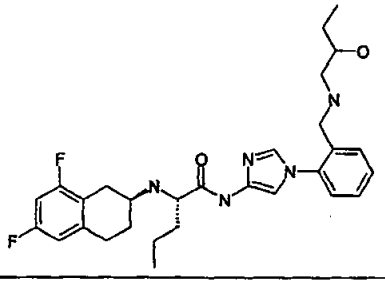
Example 155

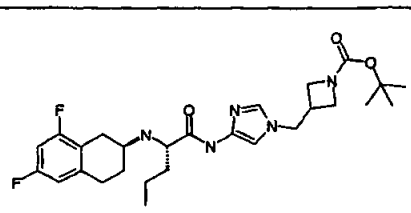
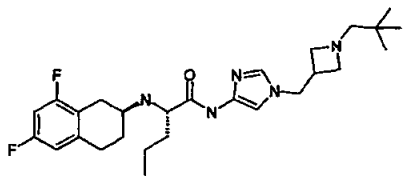
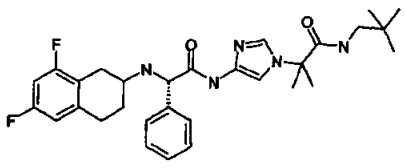
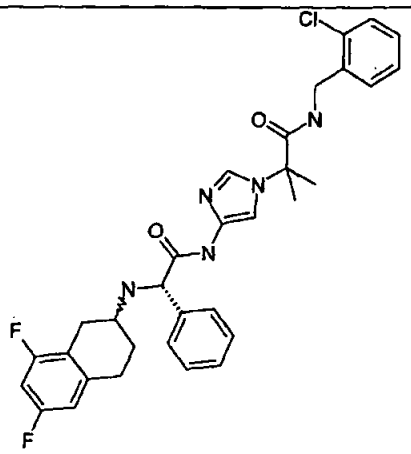
(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(2-hydroxy-butylamino)-methyl]-phenyl}-1H-imidazol-4-yl)-amide

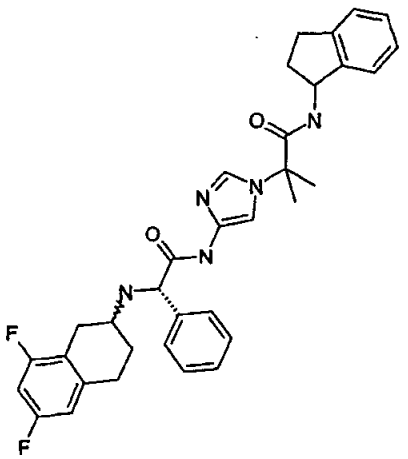
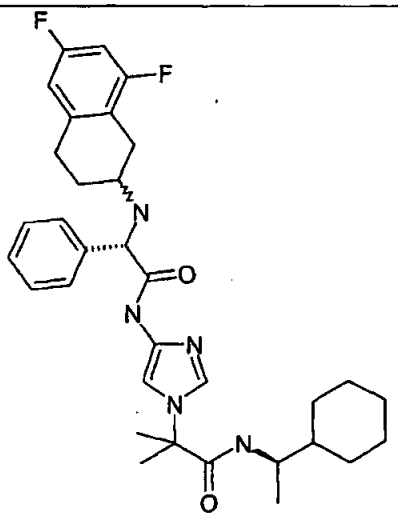
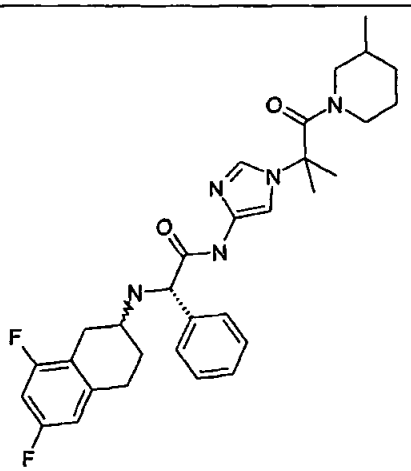
(2S)-2-(5,7-difluoro-1,2,3,4-tetrahydronaphthalen-3-ylamino)-N-(1-(2-formylphenyl)-1H-imidazol-4-yl)pentanamide was treated with the appropriate amine to afford the title compound: MS 526 m/z (M+1).

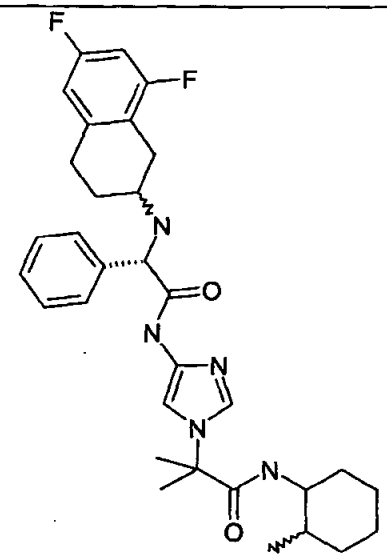
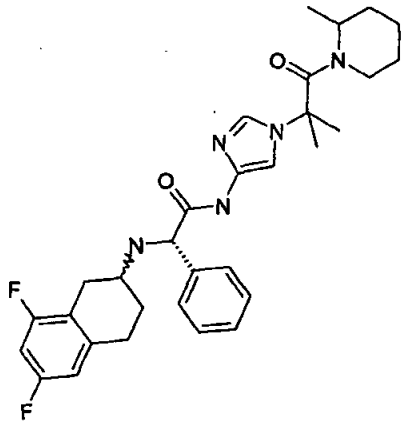
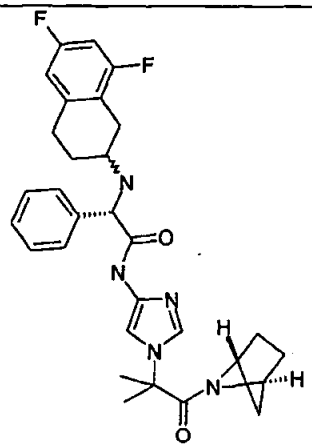
The following Examples were prepared by methods analogous to those described above.

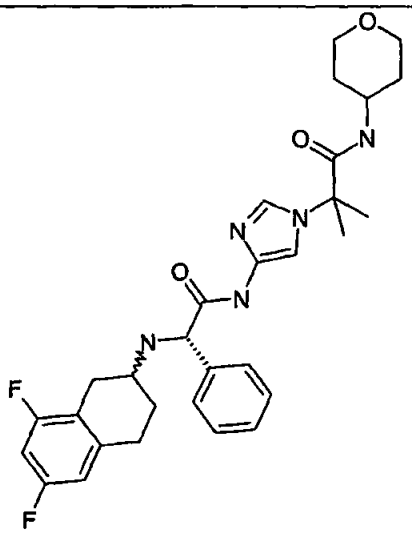
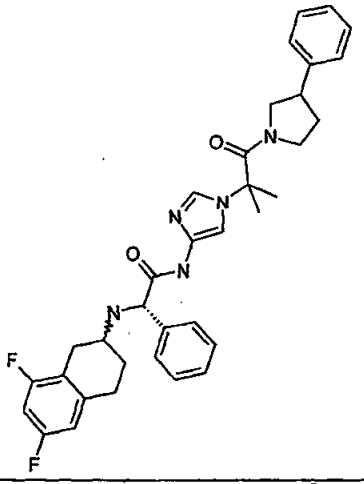
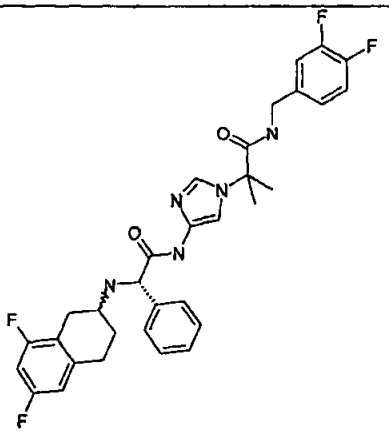
Ex	Structure	MS or NMR data	IUPACNAME
156		M+1 = 532.6	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(1-hydroxycyclohexyl)methyl]amino}-11-dimethylethyl)-1H-imidazol-4-yl]-L-norvalinamide
157		M+1 = 488.5	N-2-[(3,5-difluorophenyl)acetyl]-N-{1-[1-(piperidin-1-ylmethyl)cyclobutyl]-1H-imidazol-4-yl}-L-norvalinamide
158		M+1 = 486.5	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[1-(pyrrolidin-1-ylmethyl)cyclobutyl]-1H-imidazol-4-yl}-L-norvalinamide
159		M+1 = 490.1	N-2-[(3,5-difluorophenyl)acetyl]-N-[1-(1-{[(2,2-dimethylpropyl)amino]methyl}cyclobutyl)-1H-imidazol-4-yl]-L-norvalinamide
160		M+1 = 490.1	N-2-[(3,5-difluorophenyl)acetyl]-N-[1-(1-{[(2,2-dimethylpropyl)amino]methyl}cyclobutyl)-1H-imidazol-4-yl]-L-norvalinamide

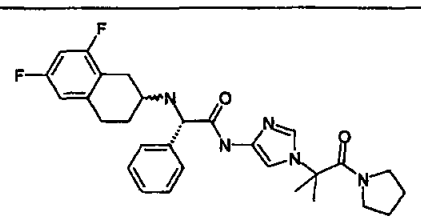
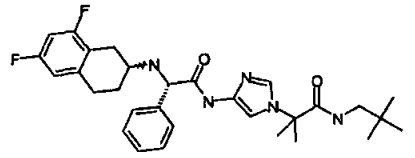
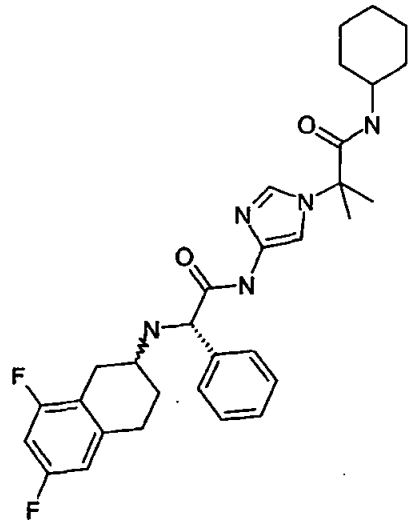
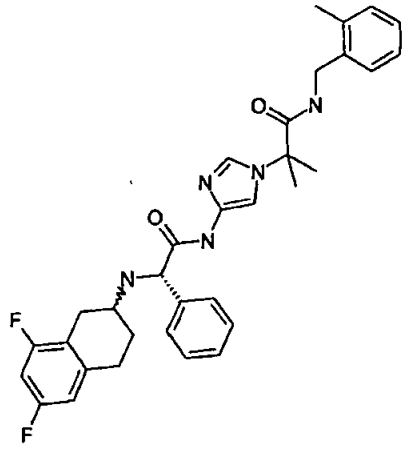
Ex	Structure	MS or NMR data	IUPACNAME
161		M+1 = 502.6	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(1-{[(22-dimethylpropyl)amino]methyl}cyclobutyl)-1H-imidazol-4-yl]-L-norvalinamide
162		M+1 = 538.26	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{1,1-dimethyl-2-[(2-methylbenzyl)amino]-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide
163		M+1 = 504.1	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{1-methyl-2-[(tetrahydro-2H-pyran-4-ylmethyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide
164		M+1 = 506.52	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(3-methoxypropyl)amino]-1,1-dimethyl-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide
165		M+1 = 526.64	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2-hydroxybutyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide

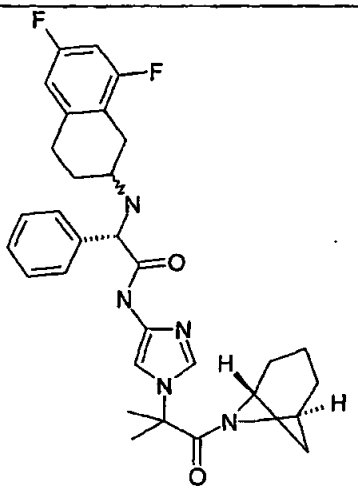
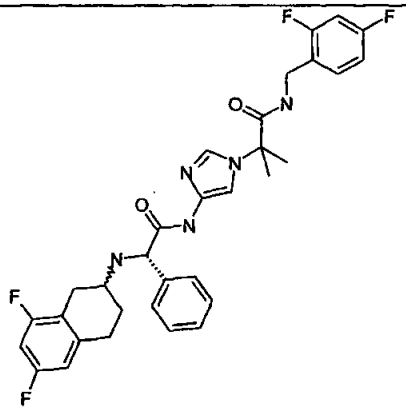
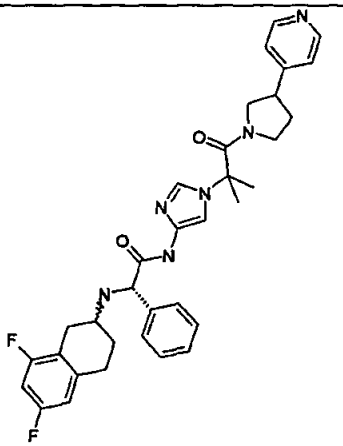
Ex	Structure	MS or NMR data	IUPACNAME
166		M+1 = 518.5	tert-butyl 3-{[4-({N-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalyl}amino)-1H-imidazol-1-yl]methyl}azetidine-1-carboxylate
167		M+1 = 488.5	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{[1-(2,2-dimethylpropyl)azetidin-3-yl]methyl}-1H-imidazol-4-yl)-L-norvalinamide
168		M+1 = 538.65	2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-N-(2,2-dimethylpropyl)-2-methylpropanamide
169		M+1 = 593.09	N-(2-chlorobenzyl)-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methylpropanamide

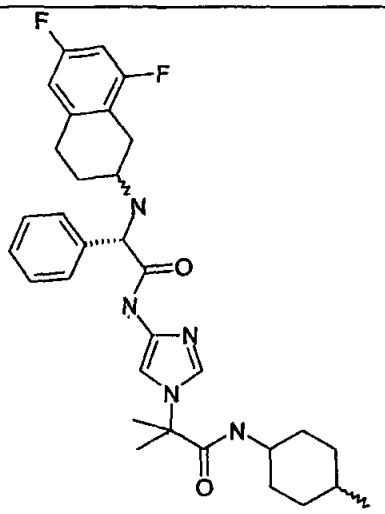
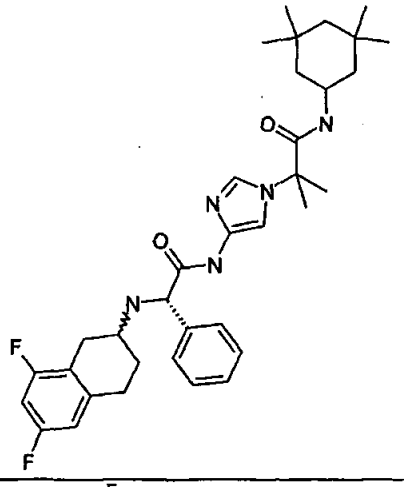
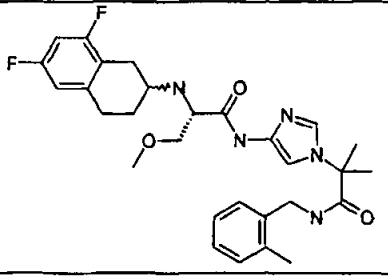
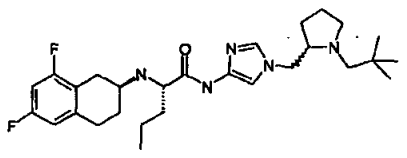
Ex	Structure	MS or NMR data	IUPACNAME
170		M+1 = 584.68	2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-N-(2,3-dihydro-1H-inden-1-yl)-2-methylpropanamide
171		M+1 = 578.72	N-[(1R)-1-cyclohexylethyl]-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methylpropanamide
172		M+1 = 550.66	(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-N-{1-[11-dimethyl-2-(3-methylpiperidin-1-yl)-2-oxoethyl]-1H-imidazol-4-yl}-2-phenylacetamide

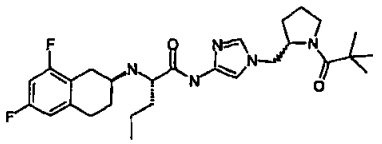
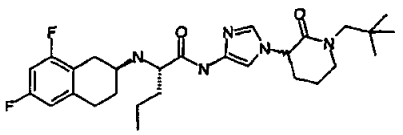
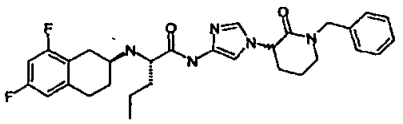
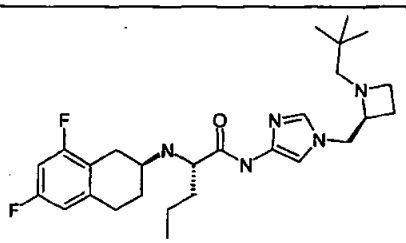
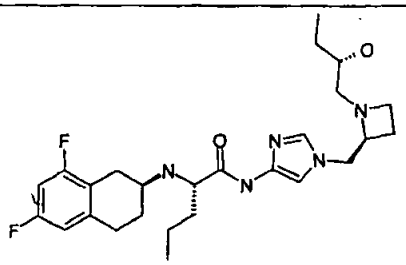
Ex	Structure	MS or NMR data	IUPACNAME
173		M+1 = 564.69	2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methyl-N-(2-methylcyclohexyl)propanamide
174		M+1 = 550.66	(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-N-{1-[1,1-dimethyl-2-(2-methylpiperidin-1-yl)-2-oxoethyl]-1H-imidazol-4-yl}-2-phenylacetamide
175		M+1 = 548.65	(2S)-N-(1-{2-[(1R, 4S)-2-azabicyclo[2.2.1]hept-2-yl]-11-dimethyl-2-oxoethyl}-1H-imidazol-4-yl)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetamide

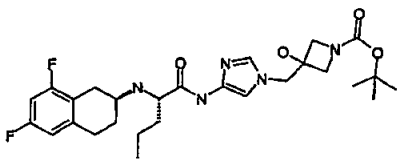
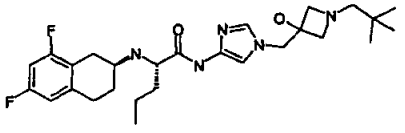
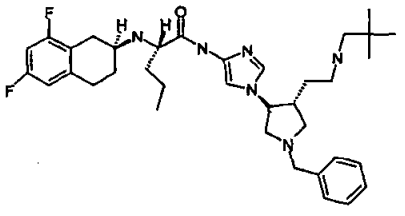
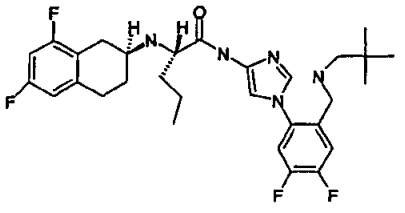
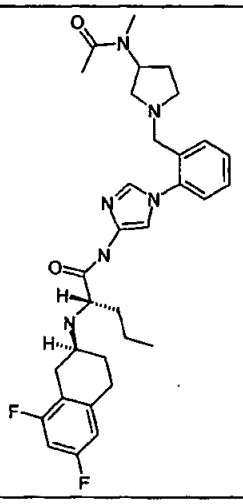
Ex	Structure	MS or NMR data	IUPACNAME
176		M+1 = 552.64	2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methyl-N-(tetrahydro-2H-pyran-4-yl)propanamide
177		M+1 = 598.71	(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-N-{1-[1,1-dimethyl-2-oxo-2-(3-phenylpyrrolidin-1-yl)ethyl]-1H-imidazol-4-yl}-2-phenylacetamide
178		M+1 = 594.62	N-(3,4-difluorobenzyl)-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methylpropanamide

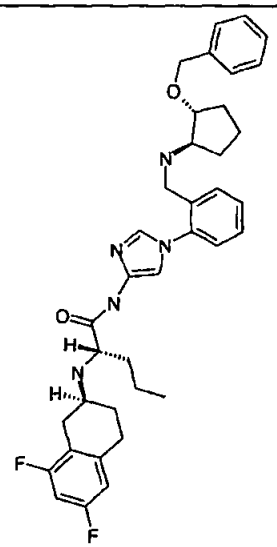
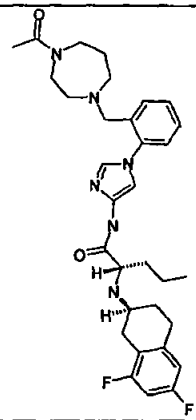
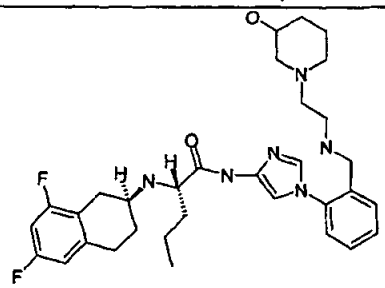
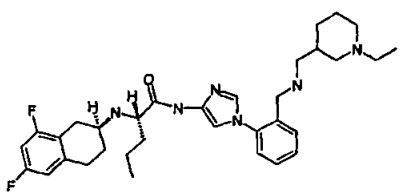
Ex	Structure	MS or NMR data	IUPACNAME
179		M+1 = 522.61	(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-N-[1-(1,1-dimethyl-2-oxo-2-pyrrolidin-1-ylethyl)-1H-imidazol-4-yl]-2-phenylacetamide
180		M+1 = 538.65	2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-N-(2,2-dimethylpropyl)-2-methylpropanamide
181		M+1 = 550.66	N-cyclohexyl-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methylpropanamide
182		M+1 = 572.67	2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methyl-N-(2-methylbenzyl)propanamide

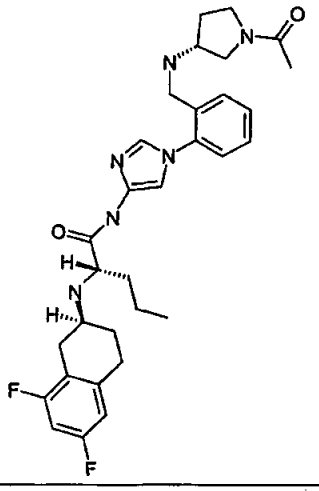
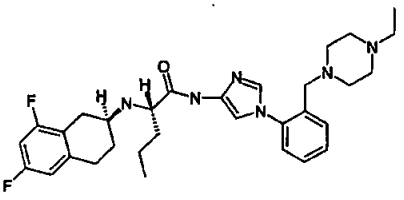
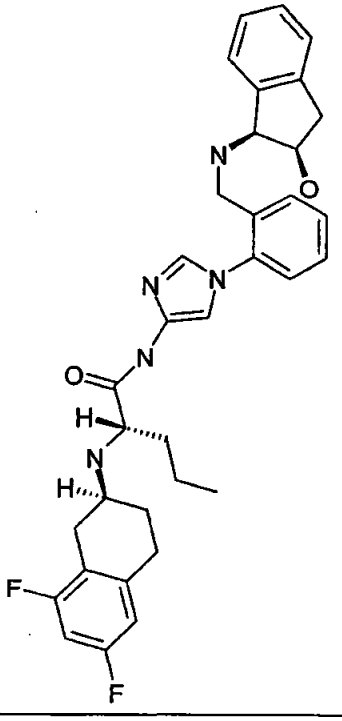
Ex	Structure	MS or NMR data	IUPACNAME
183		M+1 = 562.67	(2S)-N-(1-{2-[(1S5R)-6-azabicyclo[3.2.1]oct-6-yl]-1-1-dimethyl-2-oxoethyl}-1H-imidazol-4-yl)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetamide
184		M+1 = 594.62	N-(2,4-difluorobenzyl)-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methylpropanamide
185		M+1 = 599.69	(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-N-{1-[1,1-dimethyl-2-oxo-2-(3-pyridin-4-ylpyrrolidin-1-yl)ethyl]-1H-imidazol-4-yl}-2-phenylacetamide

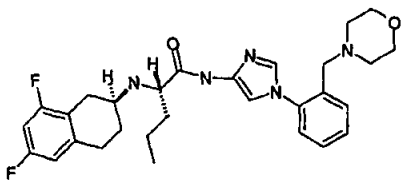
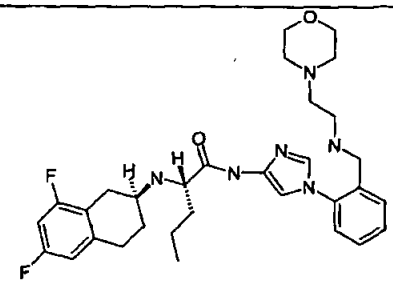
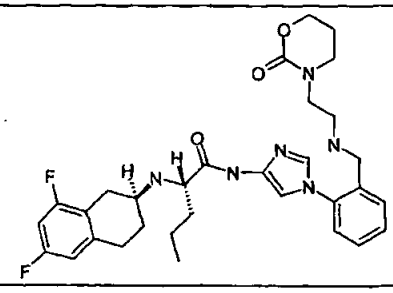
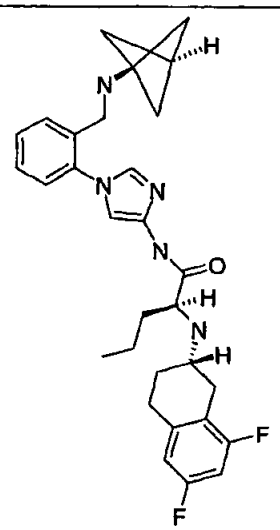
Ex	Structure	MS or NMR data	IUPACNAME
186		M+1 = 564.69	2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methyl-N-(4-methylcyclohexyl)propanamide
187		M+1 = 606.77	2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methyl-N-(3,3,5,5-tetramethylcyclohexyl)propanamide
188		M+1 = 540.04	N-2-(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)-N-(1-{1,1-dimethyl-2-[(2-methylbenzyl)amino]-2-oxoethyl}-1H-imidazol-4-yl)-O-methyl-L-serinamide
189		M+1 = 502.5	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{[1-(2,2-dimethylpropyl)pyrrolidin-2-yl]methyl}-1H-imidazol-4-yl)-L-norvalinamide

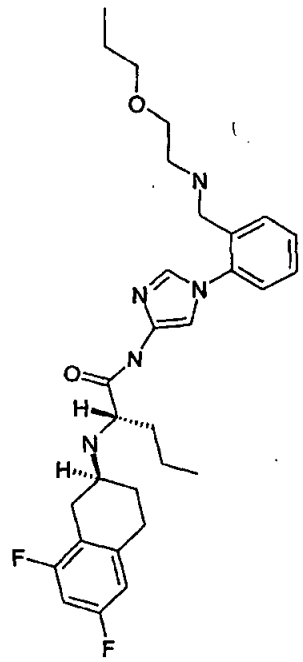
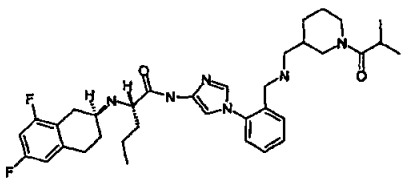
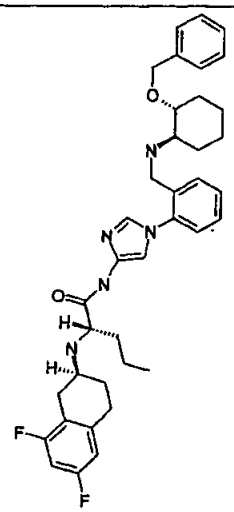
Ex	Structure	MS or NMR data	IUPACNAME
190		M+1 = 516.5	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{[1-(2,2-dimethylpropanoyl)pyrrolidin-2-yl]methyl}-1H-imidazol-4-yl)-L-norvalinamide
191		M+1 = 516.4	(2S)-2-{[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]amino}-N-{1-[1-(2,2-dimethylpropyl)-2-oxopiperidin-3-yl]-1H-imidazol-4-yl}pentanamide
192		M+1 = 536.3	(2S)-N-[1-(1-benzyl-2-oxopiperidin-3-yl)-1H-imidazol-4-yl]-2-{[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]amino}pentanamide
193		M+1 = 488.4	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{[(2S)-1-(2,2-dimethylpropyl)azetidin-2-yl]methyl}-1H-imidazol-4-yl)-L-norvalinamide
194		M+1 = 490.3	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-({(2S)-1-[(2S)-2-hydroxybutyl]azetidin-2-yl}methyl)-1H-imidazol-4-yl]-L-norvalinamide

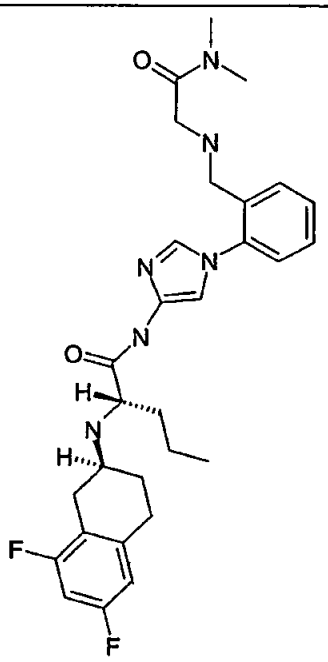
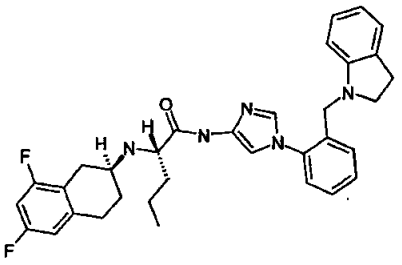
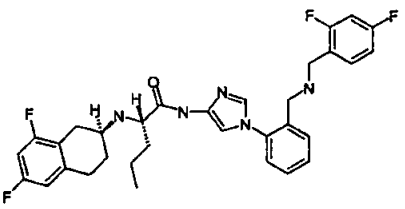
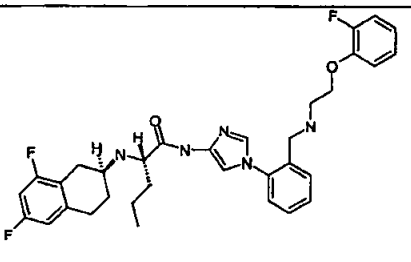
Ex	Structure	MS or NMR data	IUPACNAME
195		M+1 = 534.4	tert-butyl 3-{[4-({N-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalyl}amino)-1H-imidazol-1-yl]methyl}-3-hydroxyazetidine-1-carboxylate
196		M+1 = 504.4	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{[1-(2,2-dimethylpropyl)-3-hydroxyazetidin-3-yl]methyl}-1H-imidazol-4-yl)-L-norvalinamide
197		M+1 = 621.83	N-{1-[(3S,4R)-1-benzyl-4-{2-[(2,2-dimethylpropyl)amino]ethyl}pyrrolidin-3-yl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
198		M+1 = 560.65	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2,2-dimethylpropyl)amino]methyl}-45-difluorophenyl)-1H-imidazol-4-yl]-L-norvalinamide
199		M+1 = 579.7	N-{1-[2-({3-[acetyl(methyl)amino]pyrrolidin-1-yl}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide

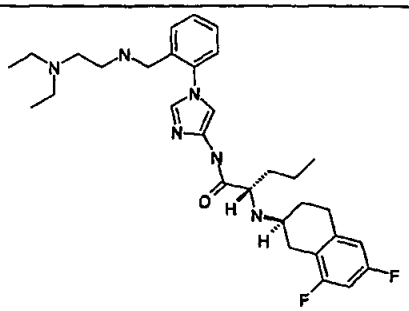
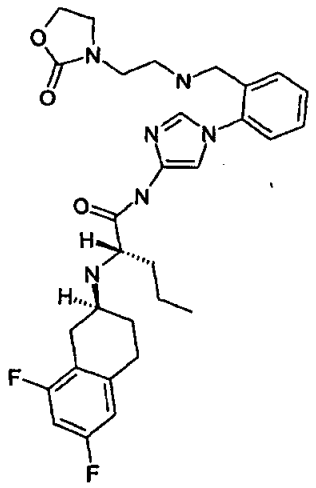
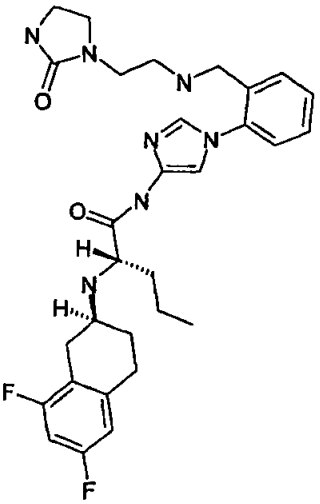
Ex	Structure	MS or NMR data	IUPACNAME
200		M+1 = 628.78	N-{1-[2-({[(1R,2R)-2-(benzyloxy)cyclopentyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
201		M+1 = 579.7	N-(1-{2-[(4-acetyl-1,4-diazepan-1-yl)methyl]phenyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
202		M+1 = 581.72	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(3-hydroxypiperidin-1-yl)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
203		M+1 = 579.75	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1-ethylpiperidin-3-yl)methyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide

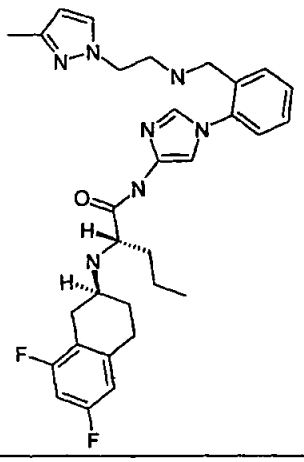
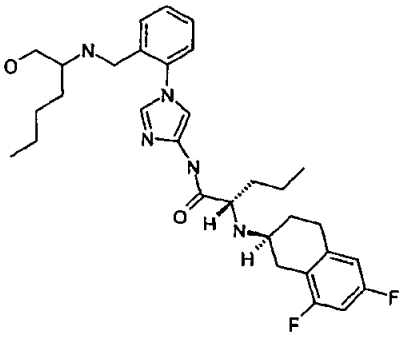
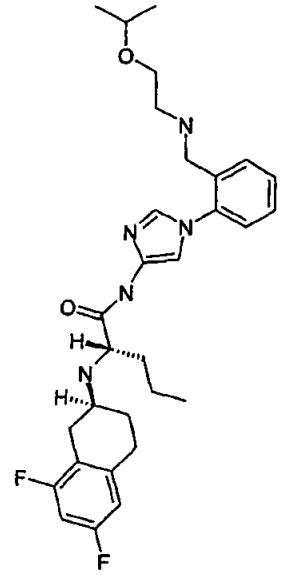
Ex	Structure	MS or NMR data	IUPACNAME
204		M+1 = 565.68	N-{1-[2-({[(3R)-1-acetylpyrrolidin-3-yl]amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
205		M+1 = 551.69	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(4-ethylpiperazin-1-yl)methyl]phenyl}-1H-imidazol-4-yl)-L-norvalinamide
206		M+1 = 586.7	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1S,2R)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide

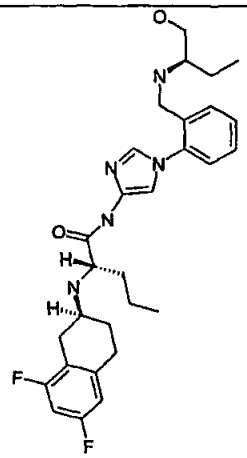
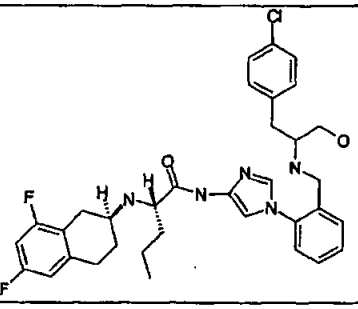
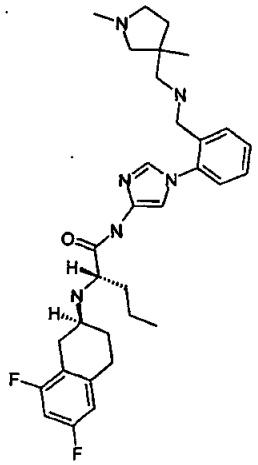
Ex	Structure	MS or NMR data	IUPACNAME
207		M+1 = 524.63	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-(morpholin-4-ylmethyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
208		M+1 = 567.69	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2-morpholin-4-ylethyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide
209		M+1 = 581.68	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(2-oxo-1,3-oxazinan-3-yl)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
210		M+1 = 520.64	N-(1-{2-[(bicyclo[1.1.1]pent-1-ylamino)methyl]phenyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide

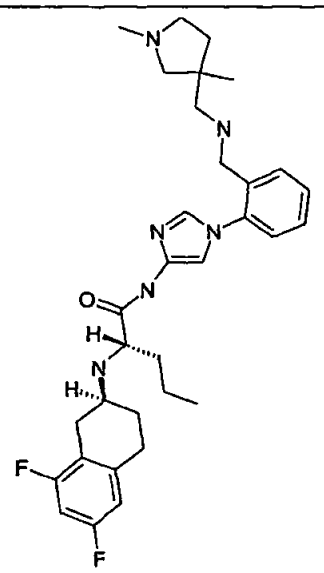
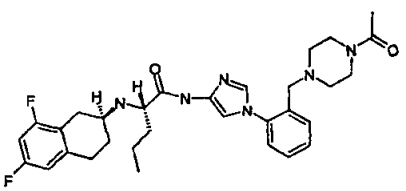
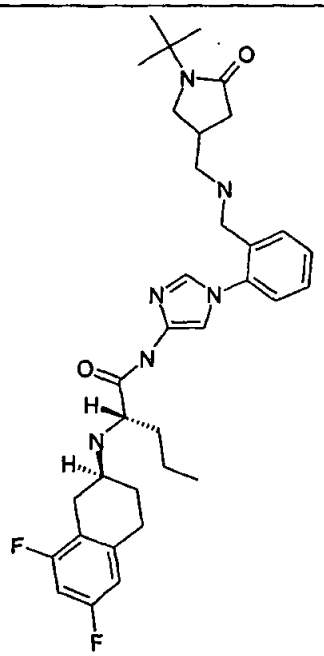
Ex	Structure	MS or NMR data	IUPACNAME
211		M+1 = 540.67	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-(2-{[(2-propoxyethyl)amino]methyl}phenyl)-1H-imidazol-4-yl}-L-norvalinamide
212		M+1 = 621.78	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1-isobutyrylpiperidin-3-yl)methyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
213		M+1 = 642.8	N-{1-[2-({[(1R,2R)-2-(benzyloxy)cyclohexyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide

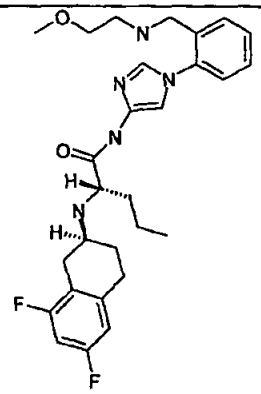
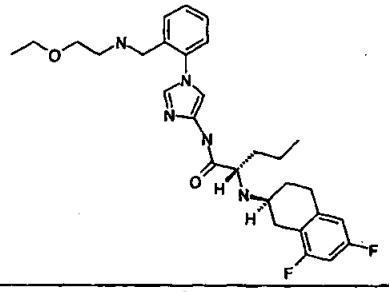
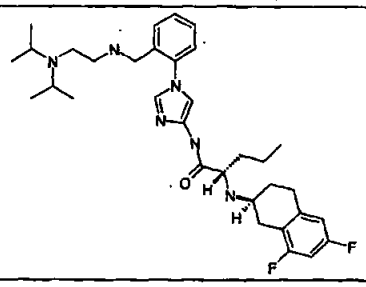
Ex	Structure	MS or NMR data	IUPACNAME
214		M+1 = 539.64	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(dimethylamino)-2-oxoethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
215		M+1 = 556.67	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-(2,3-dihydro-1H-indol-1-ylmethyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
216		M+1 = 580.64	N-[1-(2-{[(2,4-difluorobenzyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
217		M+1 = 592.67	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(2-fluorophenoxy)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide

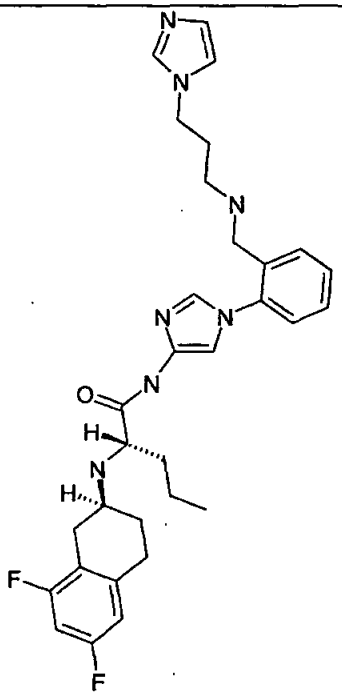
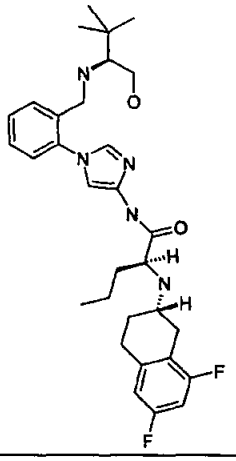
Ex	Structure	MS or NMR data	IUPACNAME
218		M+1 = 553.71	N-{1-[2-({[2-(diethylamino)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
219		M+1 = 567.65	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(2-oxo-1,3-oxazolidin-3-yl)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
220		M+1 = 566.67	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(2-oxoimidazolidin-1-yl)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide

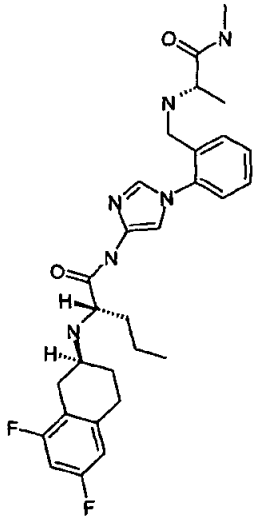
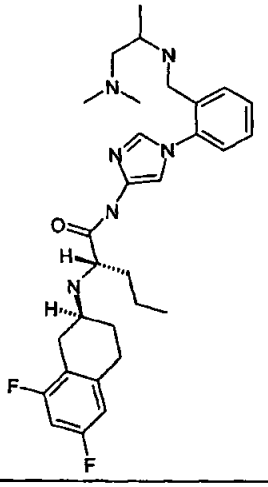
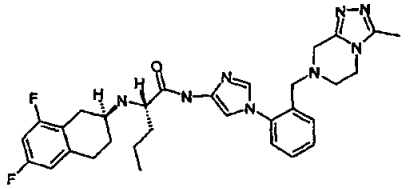
Ex	Structure	MS or NMR data	IUPACNAME
221		M+1 = 562.68	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(3-methyl-1H-pyrazol-1-yl)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
222		M+1 = 554.69	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[1-(hydroxymethyl)pentyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
223		M+1 = 540.67	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2-isopropoxyethyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide

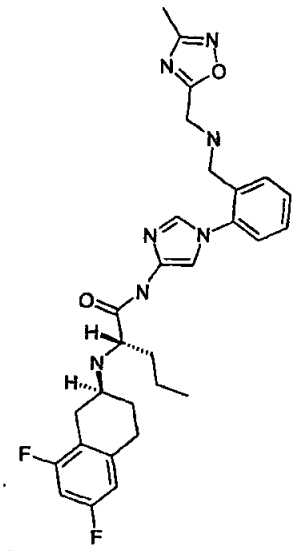
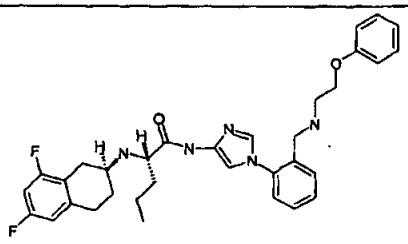
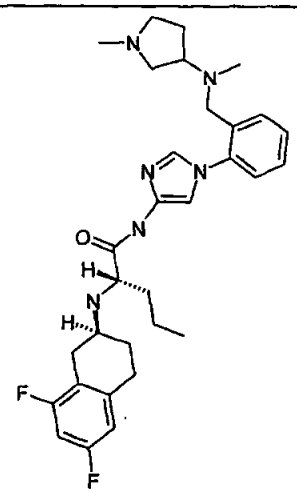
Ex	Structure	MS or NMR data	IUPACNAME
224		M+1 = 526.64	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1R)-1-(hydroxymethyl)propyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
225		M+1 = 623.16	N-{1-[2-({[1-(4-chlorobenzyl)-2-hydroxyethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
226		M+1 = 565.72	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1,3-dimethylpyrrolidin-3-yl)methyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide

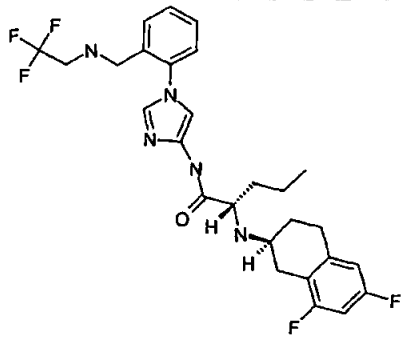
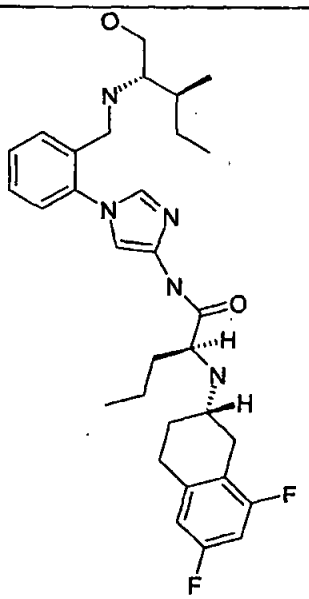
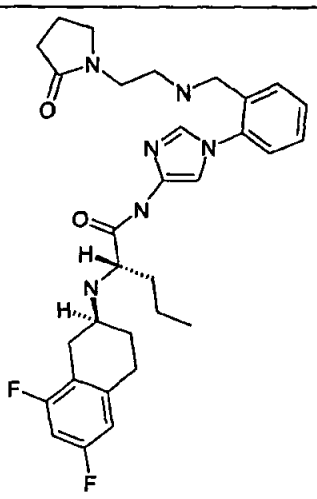
Ex	Structure	MS or NMR data	IUPACNAME
227		M+1 = 565.72	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1,3-dimethylpyrrolidin-3-yl)methyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
228		M+1 = 565.68	N-(1-{2-[(4-acetylpiperazin-1-yl)methyl]phenyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
229		M+1 = 607.76	N-{1-[2-({[(1-tert-butyl-5-oxopyrrolidin-3-yl)methyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide

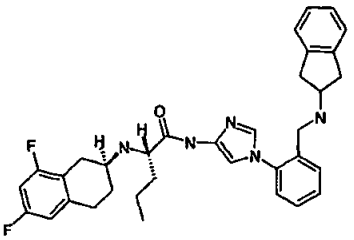
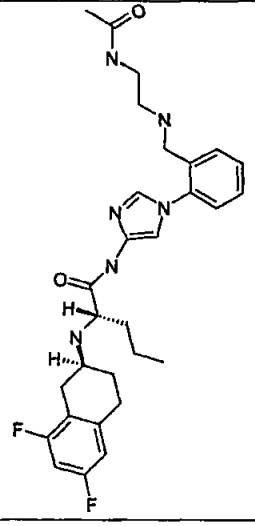
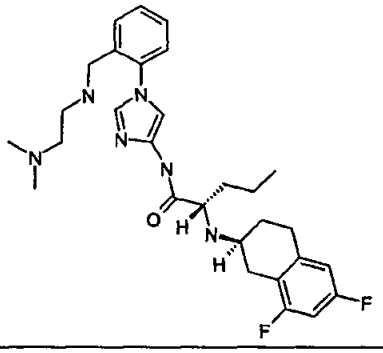
Ex	Structure	MS or NMR data	IUPACNAME
230		M+1 = 512.61	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2-methoxyethyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide
231		M+1 = 526.64	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2-ethoxyethyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide
232		M+1 = 581.76	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(diisopropylamino)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide

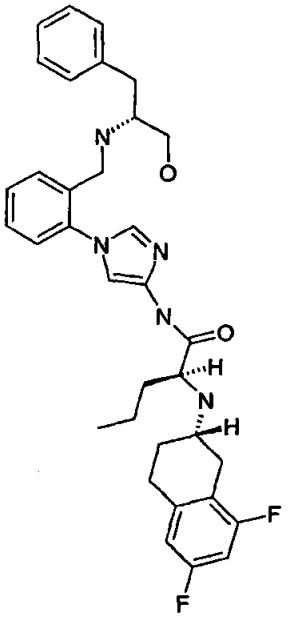
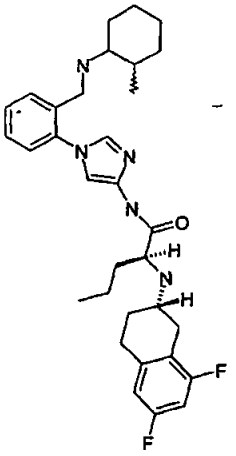
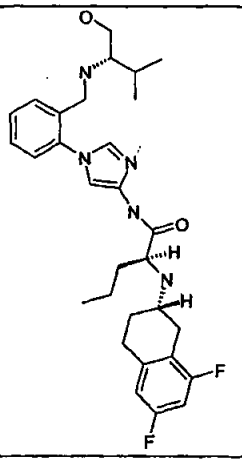
Ex	Structure	MS or NMR data	IUPACNAME
233		M+1 = 562.68	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[3-(1H-imidazol-1-yl)propyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
234		M+1 = 554.69	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1S)-1-(hydroxymethyl)-2,2-dimethylpropyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide

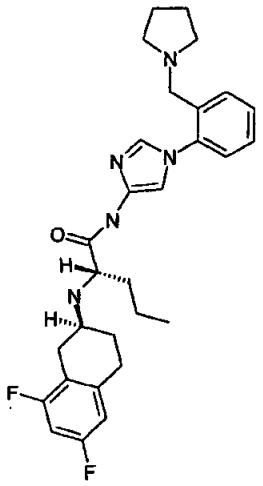
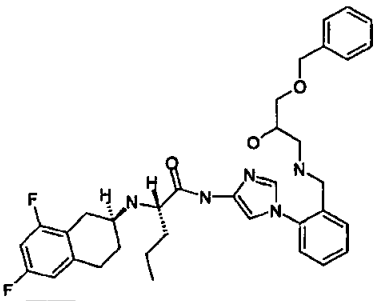
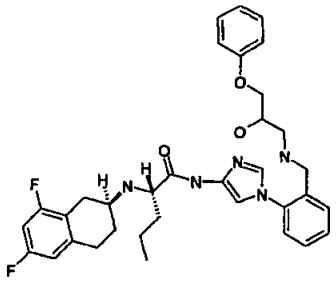
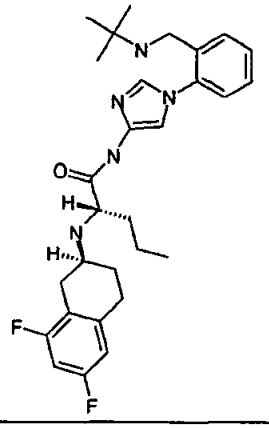
Ex	Structure	MS or NMR data	IUPACNAME
235		M+1 = 539.64	N-2-[(2S)-6,8-difluoro-1,23,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1S)-1-methyl-2-(methylamino)-2-oxoethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
236		M+1 = 539.68	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(dimethylamino)-1-methylethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
237		M+1 = 575.68	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(3-methyl-5,6-dihydro[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methyl]phenyl}-1H-imidazol-4-yl)-L-norvalinamide

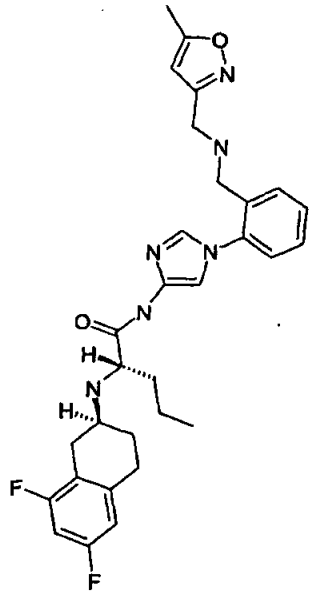
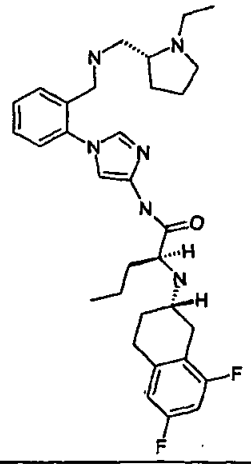
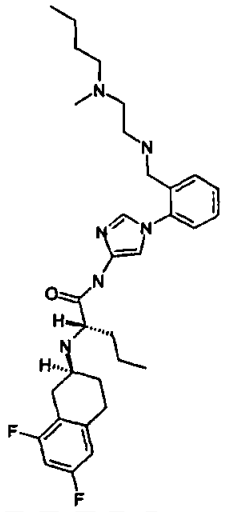
Ex	Structure	MS or NMR data	IUPACNAME
238		M+1 = 550.62	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
239		M+1 = 574.68	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2-phenoxyethyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide
240		M+1 = 551.69	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[methyl(1-methylpyrrolidin-3-yl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide

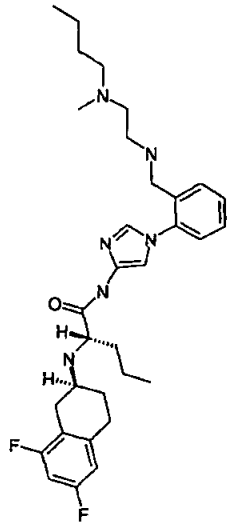
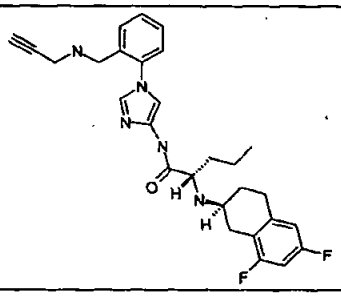
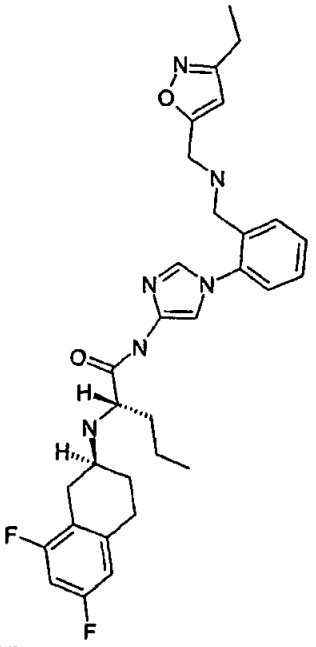
Ex	Structure	MS or NMR data	IUPACNAME
241		M+1 = 536.56	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2,2,2-trifluoroethyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide
242		M+1 = 554.69	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1S,2S)-1-(hydroxymethyl)-2-methylbutyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
243		M+1 = 565.68	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(2-oxopyrrolidin-1-yl)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide

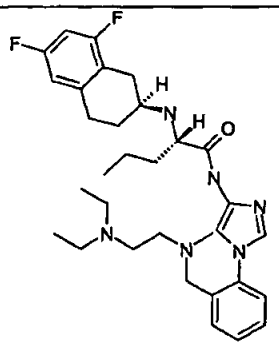
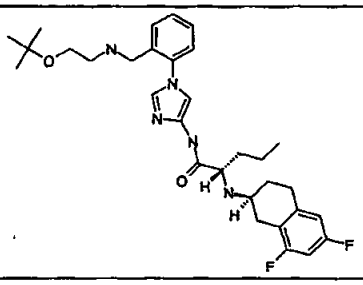
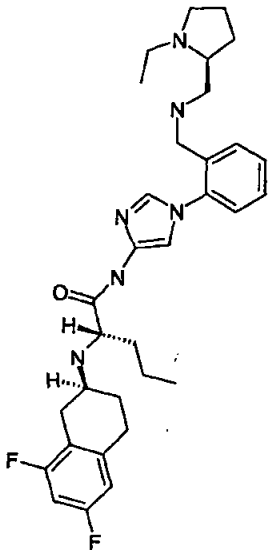
Ex	Structure	MS or NMR data	IUPACNAME
244		M+1 = 570.7	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(2,3-dihydro-1H-inden-2-ylamino)methyl]phenyl}-1H-imidazol-4-yl)-L-norvalinamide
245		M+1 = 539.64	N-{1-[2-({[2-(acetylamino)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
246		M+1 = 525.66	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(dimethylamino)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide

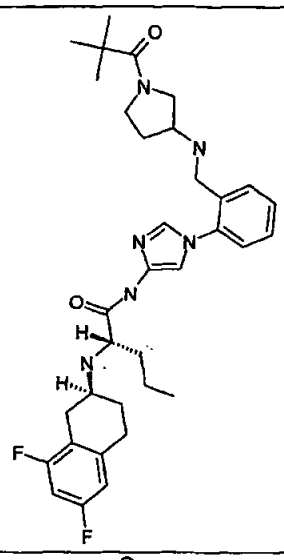
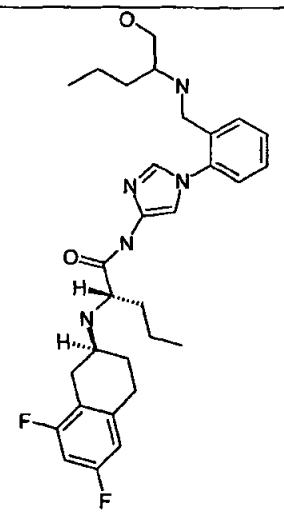
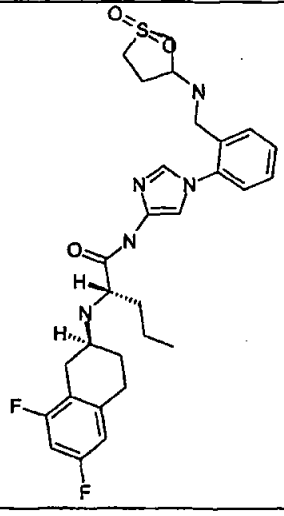
Ex	Structure	MS or NMR data	IUPACNAME
247		M+1 = 588.71	N-{1-[2-({[(1R)-1-benzyl-2-hydroxyethyl]amino}methyl) phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
248		M+1 = 550.71	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2-methylcyclohexyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide
249		M+1 = 540.67	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1S)-1-(hydroxymethyl)-2-methylpropyl]amino}methyl) phenyl]-1H-imidazol-4-yl}-L-norvalinamide

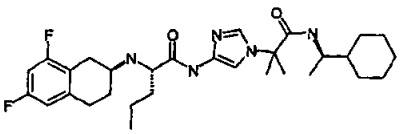
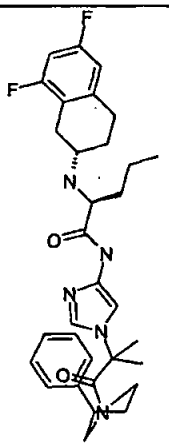
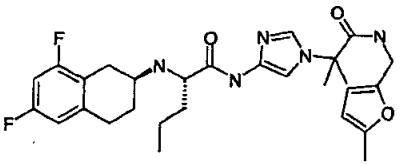
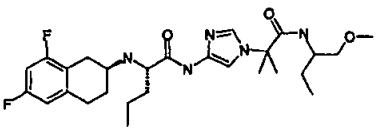
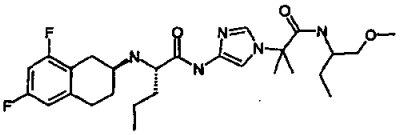
Ex	Structure	MS or NMR data	IUPACNAME
250		M+1 = 508.63	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-(pyrrolidin-1-ylmethyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
251		M+1 = 618.74	N-{1-[2-({[3-(benzyloxy)-2-hydroxypropyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
252		M+1 = 604.71	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-[[(2-hydroxy-3-phenoxypropyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide
253		M+1 = 510.64	N-(1-{2-[(tert-butylamino)methyl]phenyl}-1H-imidazol-4-yl)-N~2~-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide

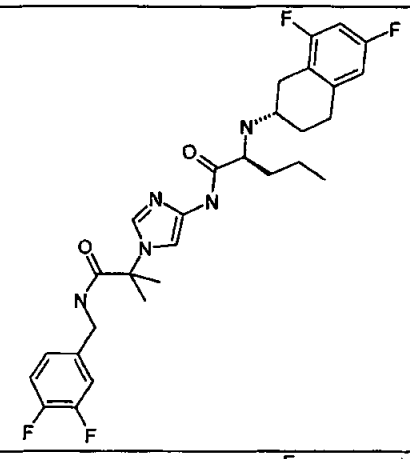
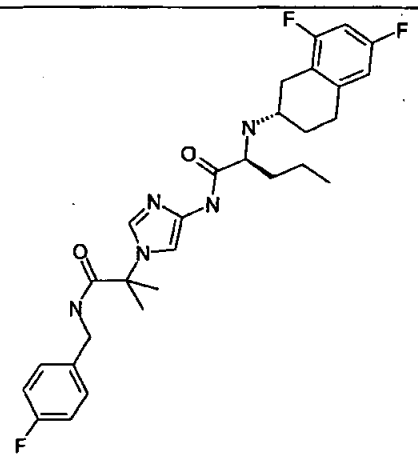
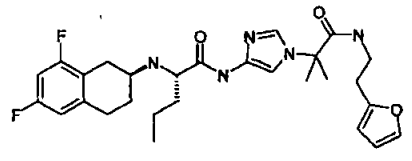
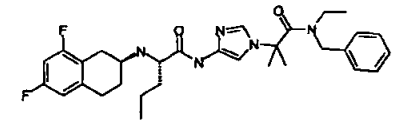
Ex	Structure	MS or NMR data	IUPACNAME
254		M+1 = 549.64	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(5-methylisoxazol-3-yl)methyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
255		M+1 = 565.72	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[({[(2R)-1-ethylpyrrolidin-2-yl]methyl}amino)methyl]phenyl}-1H-imidazol-4-yl)-L-norvalinamide
256		M+1 = 567.74	N-(1-{2-[({2-[butyl(methyl)amino]ethyl}amino)methyl]phenyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide

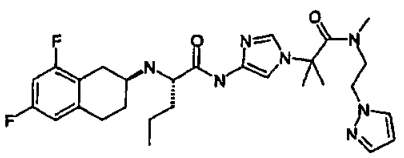
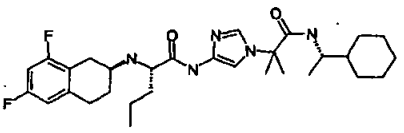
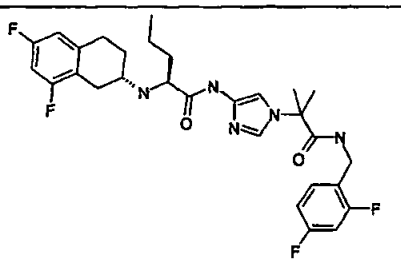
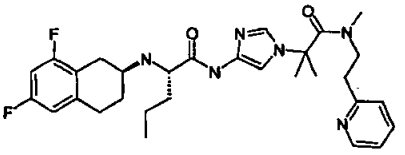
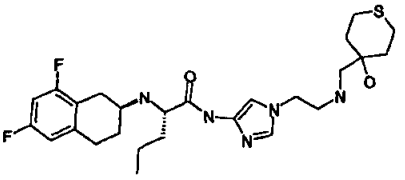
Ex	Structure	MS or NMR data	IUPACNAME
257		M+1 = 567.74	N-(1-{2-[({2-[butyl(methyl)amino]ethyl}amino)methyl]phenyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
258		M+1 = 492.58	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(prop-2-yn-1-ylamino)methyl]phenyl}-1H-imidazol-4-yl)-L-norvalinamide
259		M+1 = 563.66	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(3-ethylisoxazol-5-yl)methyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide

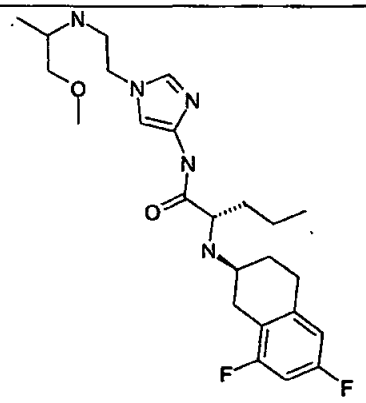
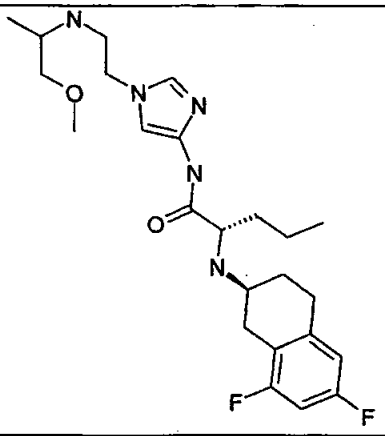
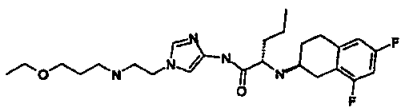
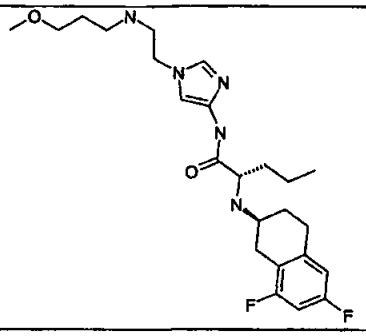
Ex	Structure	MS or NMR data	IUPACNAME
260		M+1 = 567.74	N-{1-[2-({[2-(diethylamino)ethyl](methyl)amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
261		M+1 = 554.69	N-[1-(2-{[(2-tert-butoxyethyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
262		M+1 = 565.72	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[({[(2S)-1-ethylpyrrolidin-2-yl]methyl}amino)methyl]phenyl}-1H-imidazol-4-yl)-L-norvalinamide

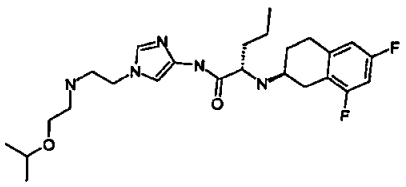
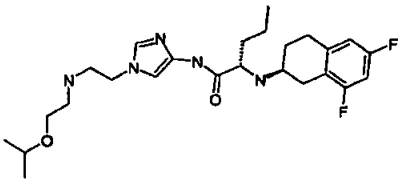
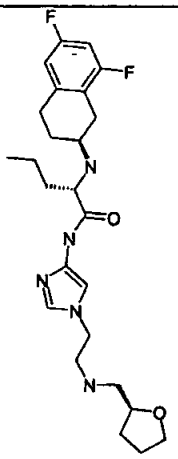
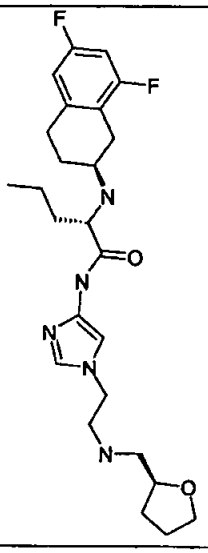
Ex	Structure	MS or NMR data	IUPACNAME
263		M+1 = 607.76	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
264		M+1 = 540.67	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[1-(hydroxymethyl)butyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
265		M+1 = 572.69	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(1,1-dioxidotetrahydro-3-thienyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide

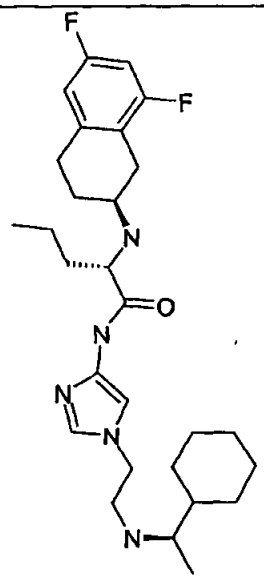
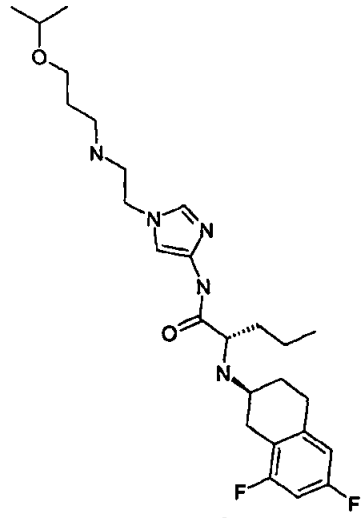
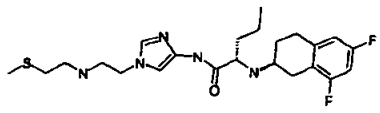
Ex	Structure	MS or NMR data	IUPACNAME
266		M+1 = 544.28	N-[1-(2-{[(1R)-1-cyclohexylethyl]amino}-1,1-dimethyl-2-oxoethyl)-1H-imidazol-4-yl]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
267		M+1 = 564.29	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[1,1-dimethyl-2-oxo-2-(3-phenylpyrrolidin-1-yl)ethyl]-1H-imidazol-4-yl}-L-norvalinamide
268		M+1 = 528.25	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(1,1-dimethyl-2-{[(5-methyl-2-furyl)methyl]amino}-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide
269		M+1 = 520.3	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[1-(methoxymethyl)propyl]amino}-1,1-dimethyl-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide
270		M+1 = 520.28	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[1-(methoxymethyl)propyl]amino}-1,1-dimethyl-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide

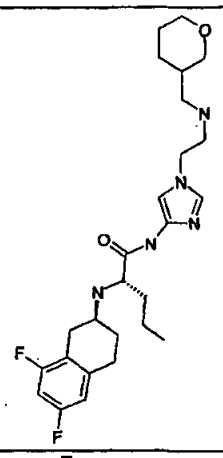
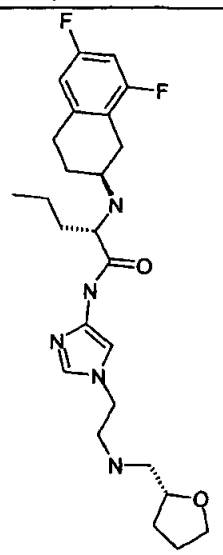
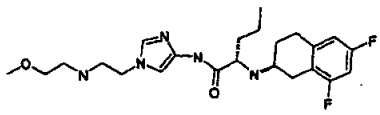
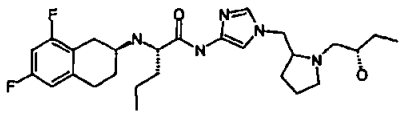
Ex	Structure	MS or NMR data	IUPACNAME
271		M+1 = 560.22	N-(1-{2-[(3,4-difluorobenzyl)amino]-1,1-dimethyl-2-oxoethyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
272		M+1 = 542.25	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(4-fluorobenzyl)amino]-1,1-dimethyl-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide
273		M+1 = 528.28	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[2-(2-furyl)ethyl]amino}-1,1-dimethyl-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide
274		M+1 = 552.12	N-(1-{2-[benzyl(ethyl)amino]-1,1-dimethyl-2-oxoethyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide

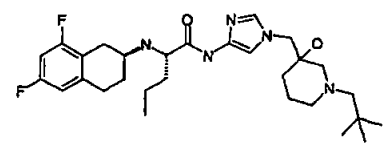
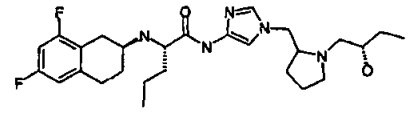
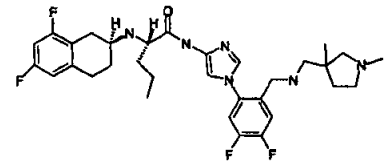
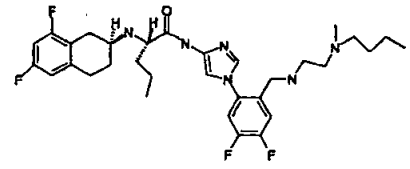
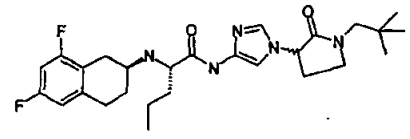
Ex	Structure	MS or NMR data	IUPACNAME
275		M+1 = 548.25	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(1,1-dimethyl-2-{methyl[2-(1H-pyrazol-1-yl)ethyl]amino}-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide
276		M+1 = 544.31	N-[1-(2-{[(1S)-1-cyclohexylethyl]amino}-1,1-dimethyl-2-oxoethyl)-1H-imidazol-4-yl]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
277		M+1 = 560.2	N-(1-{2-[(2,4-difluorobenzyl)amino]-1,1-dimethyl-2-oxoethyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
278		M+1 = 553.23	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{1,1-dimethyl-2-[methyl(2-pyridin-2-ylethyl)amino]-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide
279		data not available	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(4-hydroxytetrahydro-2H-thiopyran-4-yl)methyl]amino}ethyl)-1H-imidazol-4-yl]-L-norvalinamide

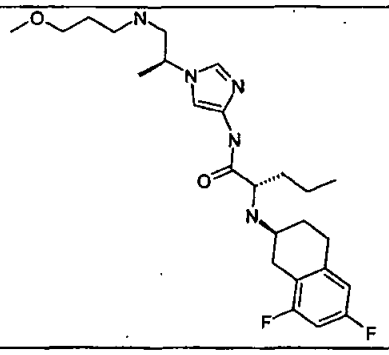
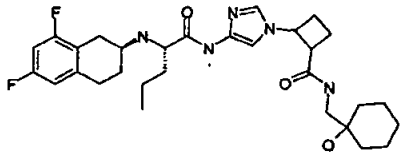
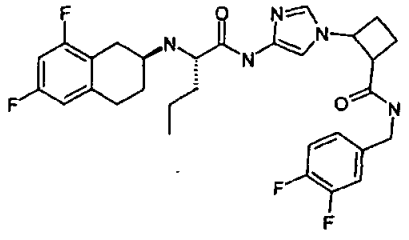
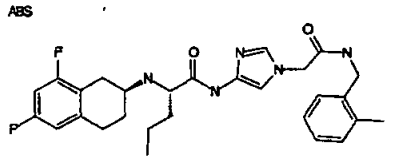
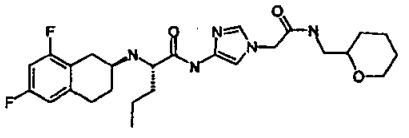
Ex	Structure	MS or NMR data	IUPACNAME
280		M+1 = 464.2	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(2-methoxy-1-methylethyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide
281		data not available	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(2-methoxy-1-methylethyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide
282		data not available	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(3-ethoxypropyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide
283		M+1 = 464.3	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(3-methoxypropyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide

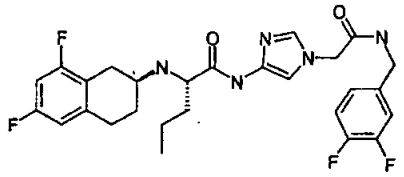
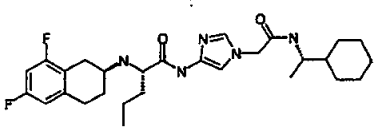
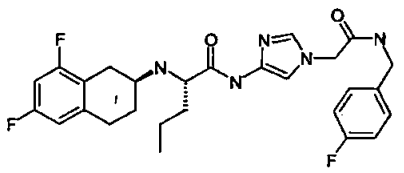
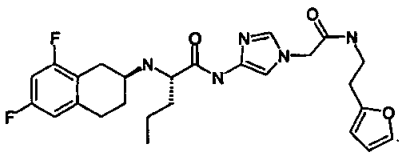
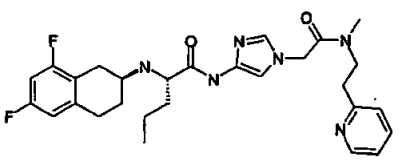
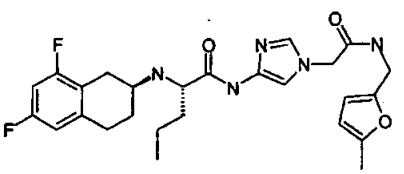
Ex	Structure	MS or NMR data	IUPACNAME
284		M+1 = 478.3	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(2-isopropoxyethyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide
285		data not available	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(2-isopropoxyethyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide
286		M+1 = 476.3	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2S)-tetrahydrofuran-2-ylmethyl]amino}ethyl)-1H-imidazol-4-yl]-L-norvalinamide
287		data not available	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2S)-tetrahydrofuran-2-ylmethyl]amino}ethyl)-1H-imidazol-4-yl]-L-norvalinamide

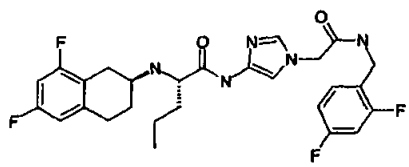
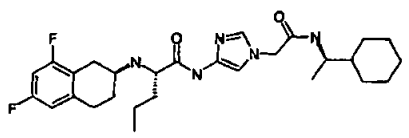
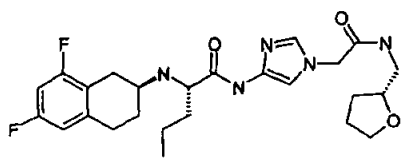
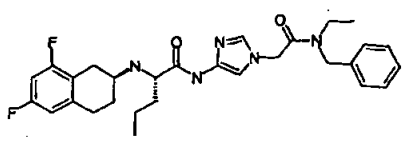
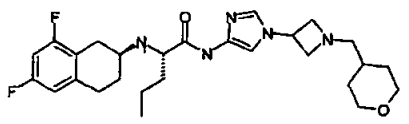
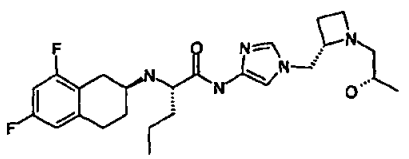
Ex	Structure	MS or NMR data	IUPACNAME
288		data not available	N-[1-(2-{[(1R)-1-cyclohexylethyl]amino}ethyl)-1H-imidazol-4-yl]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
289		data not available	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(3-isopropoxypropyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide
290		data not available	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[2-(methylthio)ethyl]amino}ethyl)-1H-imidazol-4-yl]-L-norvalinamide

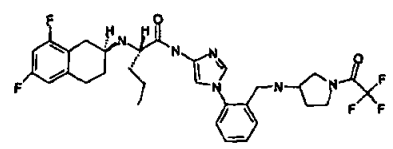
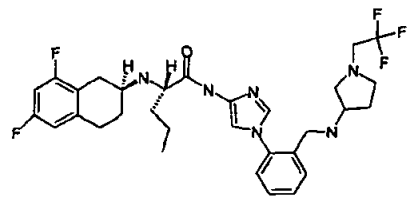
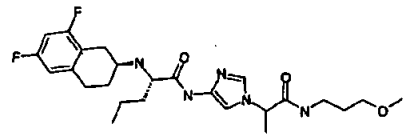
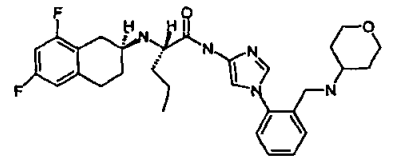
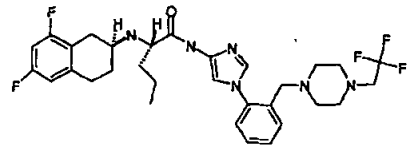
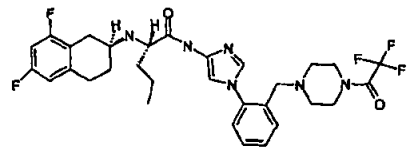
Ex	Structure	MS or NMR data	IUPACNAME
291		data not available	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(tetrahydro-2H-pyran-3-ylmethyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide
292		data not available	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2R)-tetrahydrofuran-2-ylmethyl]amino}ethyl)-1H-imidazol-4-yl]-L-norvalinamide
293		data not available	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(2-methoxyethyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide
294		M+1 = 504.4	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-({1-[(2S)-2-hydroxybutyl]pyrrolidin-2-yl}methyl)-1H-imidazol-4-yl]-L-norvalinamide

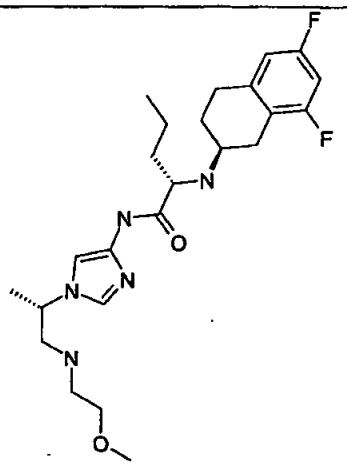
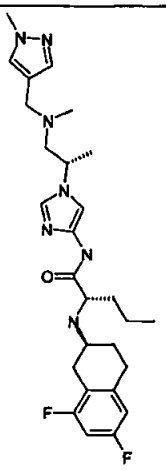
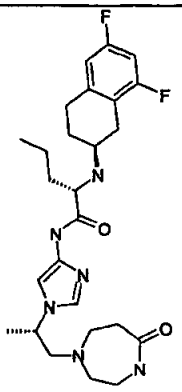
Ex	Structure	MS or NMR data	IUPACNAME
295		M+1 = 532.5	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{[1-(2,2-dimethylpropyl)-3-hydroxypiperidin-3-yl]methyl}-1H-imidazol-4-yl)-L-norvalinamide
296		M+1 = 504.4	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-({1-[(2S)-2-hydroxybutyl]pyrrolidin-2-yl}methyl)-1H-imidazol-4-yl]-L-norvalinamide
297		M+1 = 601.7	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1,3-dimethylpyrrolidin-3-yl)methyl]amino}methyl)-4,5-difluorophenyl]-1H-imidazol-4-yl}-L-norvalinamide
298*		M+1 = 603.72	N-(1-{2-[({2-[butyl(methyl)amino]ethyl}amino)methyl]-45-difluorophenyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
299		M+1 = 502.3	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[1-(2,2-dimethylpropyl)-2-oxopyrrolidin-3-yl]-1H-imidazol-4-yl}-L-norvalinamide

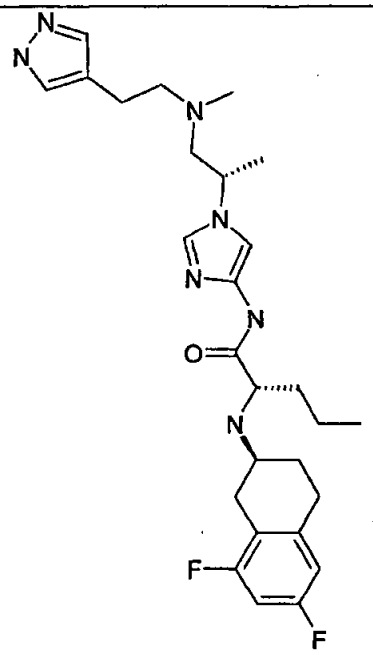
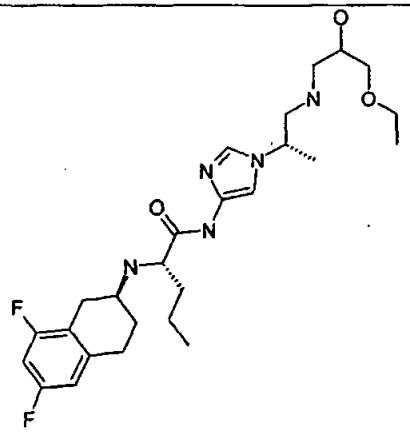
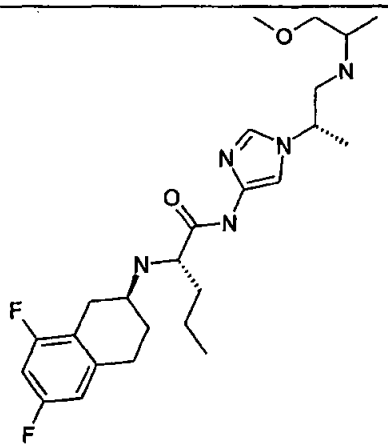
Ex	Structure	MS or NMR data	IUPACNAME
300		M+1 = 478.3	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{(1S)-2-[(3-methoxypropyl)amino]-1-methylethyl}-1H-imidazol-4-yl)-L-norvalinamide
301		M+1 = 558.3	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1-hydroxycyclohexyl)methyl]amino}carbonyl)cyclobutyl]-1H-imidazol-4-yl}-L-norvalinamide
302		M+1 = 572.29	N-[1-(2-{[(3,4-difluorobenzyl)amino]carbonyl}cyclobutyl)-1H-imidazol-4-yl]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
303		M+1 = 510.23	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(2-methylbenzyl)amino]-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide
304		M+1 = 504.26	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-oxo-2-[(tetrahydro-2H-pyran-2-ylmethyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide

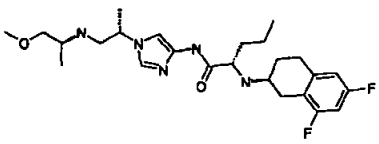
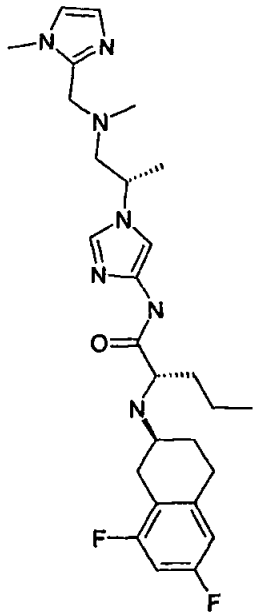
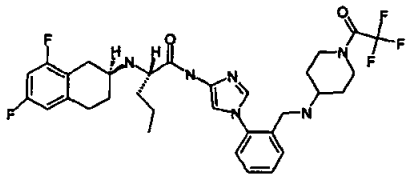
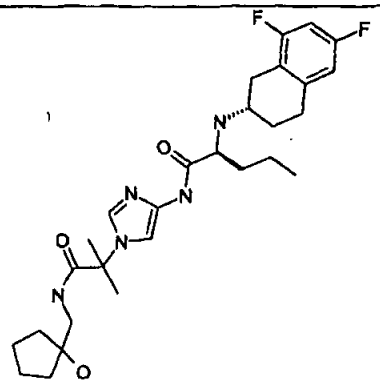
Ex	Structure	MS or NMR data	IUPACNAME
305		M+1 = 532.22	N-(1-{2-[(34-difluorobenzyl)amino]-2-oxoethyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
306		M+1 = 516.29	N-[1-(2-{[(1S)-1-cyclohexylethyl]amino}-2-oxoethyl)-1H-imidazol-4-yl]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
307		M+1 = 514.22	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(4-fluorobenzyl)amino]-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide
308		M+1 = 500.22	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[2-(2-furyl)ethyl]amino}-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide
309		M+1 = 525.23	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[methyl(2-pyridin-2-ylethyl)amino]-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide
310		M+1 = 500.22	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(5-methyl-2-furyl)methyl]amino}-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide

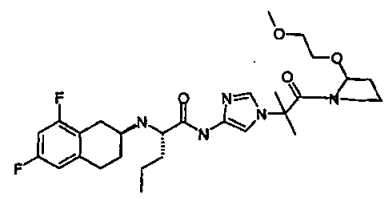
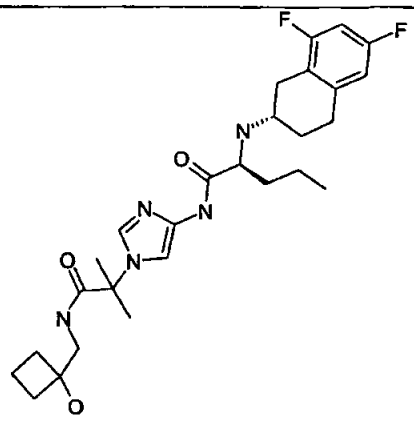
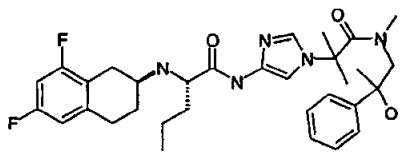
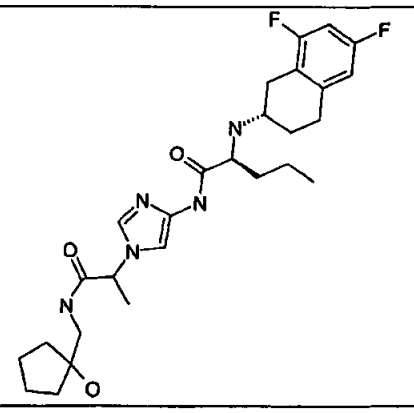
Ex	Structure	MS or NMR data	IUPACNAME
311		M+1 = 532.21	N-(1-{2-[(24-difluorobenzyl)amino]-2-oxoethyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
312		M+1 = 516.3	N-[1-(2-{[(1R)-1-cyclohexylethyl]amino}-2-oxoethyl)-1H-imidazol-4-yl]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
313		M+1 = 490.26	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-oxo-2-{[(2R)-tetrahydrofuran-2-ylmethyl]amino}ethyl)-1H-imidazol-4-yl]-L-norvalinamide
314		M+1 = 524.27	N-(1-{2-[benzyl(ethyl)amino]-2-oxoethyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
315		M+1 = 502.2	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[1-(tetrahydro-2H-pyran-4-ylmethyl)azetidin-3-yl]-1H-imidazol-4-yl}-L-norvalinamide
316		M+1 = 476.3	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-({(2S)-1-[(2S)-2-hydroxypropyl]azetidin-2-yl}methyl)-1H-imidazol-4-yl]-L-norvalinamide

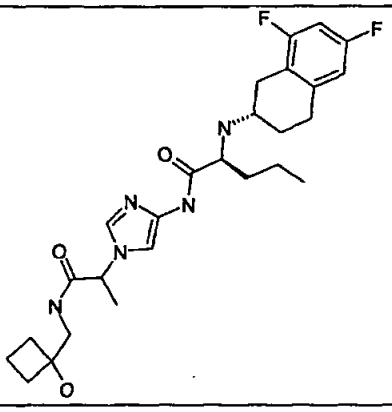
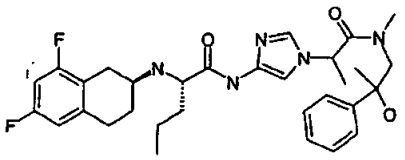
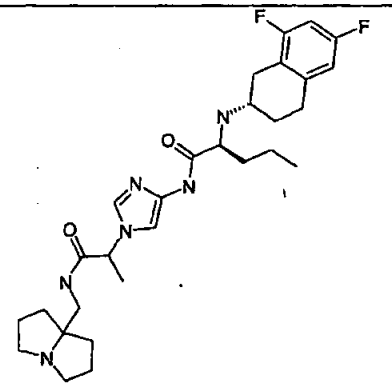
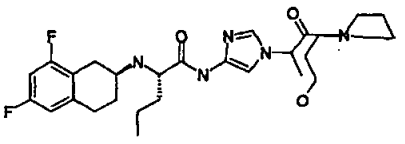
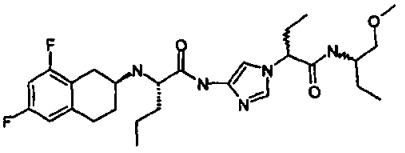
Ex	Structure	MS or NMR data	IUPACNAME
317		M+1 = 619.65	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[1-(trifluoroacetyl)pyrrolidin-3-yl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
318		M+1 = 605.66	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[1-(2,2,2-trifluoroethyl)pyrrolidin-3-yl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
319		M+1 = 492.1	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(3-methoxypropyl)amino]-1-methyl-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide
320		M+1 = 538.65	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(tetrahydro-2H-pyran-4-ylamino)methyl]phenyl}-1H-imidazol-4-yl)-L-norvalinamide
321		M+1 = 605.66	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[4-(2,2,2-trifluoroethyl)piperazin-1-yl]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide
322		M+1 = 619.65	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[4-(trifluoroacetyl)piperazin-1-yl]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide

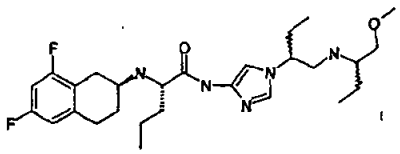
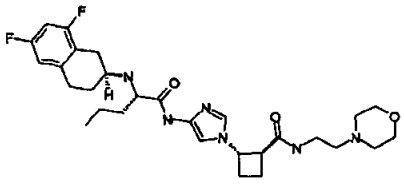
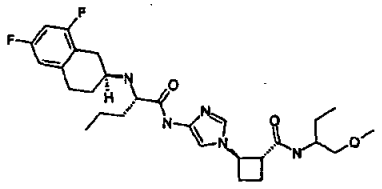
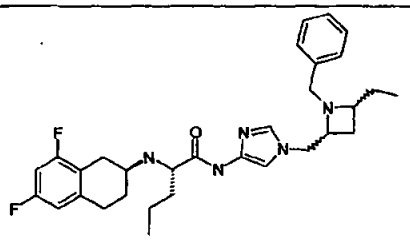
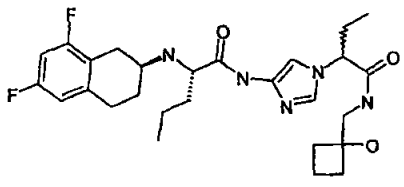
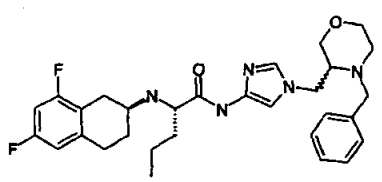
Ex	Structure	MS or NMR data	IUPACNAME
323		M+1 = 465.19	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{(1S)-2-[(2-methoxyethyl)amino]-1-methylethyl}-1H-imidazol-4-yl)-L-norvalinamide
324		M+1 = 514.25	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[(1S)-1-methyl-2-{methyl[(1-methyl-1H-pyrazol-4-yl)methyl]amino}ethyl]-1H-imidazol-4-yl}-L-norvalinamide
325		M+1 = 503.14	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[(1S)-1-methyl-2-(5-oxo-14-diazepan-1-yl)ethyl]-1H-imidazol-4-yl}-L-norvalinamide

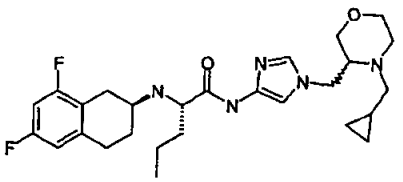
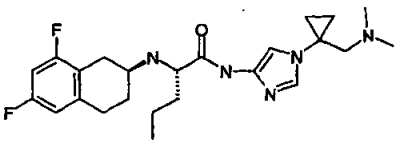
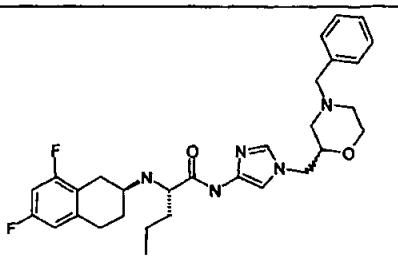
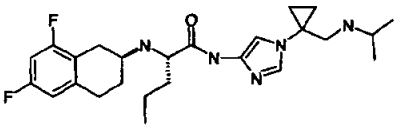
Ex	Structure	MS or NMR data	IUPACNAME
326		M+1 = 514.25	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[(1S)-1-methyl-2-{methyl[2-(1H-pyrazol-4-yl)ethyl]amino}ethyl]-1H-imidazol-4-yl}-L-norvalinamide
327		M+1 = 508.34	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{(1S)-2-[(3-ethoxy-2-hydroxypropyl)amino]-1-methylethyl}-1H-imidazol-4-yl)-L-norvalinamide
328		M+1 = 478.28	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{(1S)-2-[(2-methoxy-1-methylethyl)amino]-1-methylethyl}-1H-imidazol-4-yl)-L-norvalinamide

Ex	Structure	MS or NMR data	IUPACNAME
329		M+1 = 478.22	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[(1S)-2-{[(1S)-2-methoxy-1-methylethyl]amino}-1-methylethyl]-1H-imidazol-4-yl}-L-norvalinamide
330		M+1 = 514.14	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[(1S)-1-methyl-2-{methyl[(1-methyl-1H-imidazol-2-yl)methyl]amino}ethyl]-1H-imidazol-4-yl}-L-norvalinamide
331		M+1 = 633.67	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[1-(trifluoroacetyl)piperidin-4-yl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide
332		M+1 = 532.4	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(1-hydroxycyclopentyl)methyl]amino}-1,1-dimethyl-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide

Ex	Structure	MS or NMR data	IUPACNAME
333		M+1 = 575.95	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[4-(2-methoxyethoxy)piperidin-1-yl]-1,1-dimethyl-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide
334		M+1 = 518.23	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(1-hydroxycyclobutyl)methyl]amino}-1,1-dimethyl-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide
335		M+1 = 582.29	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(2-hydroxy-2-phenylpropyl)(methyl)amino]-1,1-dimethyl-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide
336		M+1 = 518.22	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(1-hydroxycyclopentyl)methyl]amino}-1-methyl-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide

Ex	Structure	MS or NMR data	IUPACNAME
337		M+1 = 504.17	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(1-hydroxycyclobutyl)methyl]amino}-1-methyl-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide
338		M+1 = 568.23	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(2-hydroxy-2-phenylpropyl)(methyl)amino]-1-methyl-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide
339		M+1 = 543.21	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{1-methyl-2-oxo-2-[(tetrahydro-1H-pyrrolizin-7a(5H)-ylmethyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide
340		M+1 = 532.21	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[2-(2-hydroxyethyl)piperidin-1-yl]-1-methyl-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide
341		M+1 = 520.2	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[1-({[1-(methoxymethyl)propyl]amino}carbonyl)propyl]-1H-imidazol-4-yl}-L-norvalinamide

Ex	Structure	MS or NMR data	IUPACNAME
342		M+1 = 506.1	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[1-({[1-(methoxymethyl)propyl]amino}methyl)propyl]-1H-imidazol-4-yl}-L-norvalinamide
343		M+1 = 559.1	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[(1S,2S)-2-{[(2-morpholin-4-ylethyl)amino]carbonyl}cyclobutyl]-1H-imidazol-4-yl}-L-norvalinamide
344		M+1 = 532.1	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[(1R,2R)-2-({[1-(methoxymethyl)propyl]amino}carbonyl)cyclobutyl]-1H-imidazol-4-yl}-L-norvalinamide
345		M+1 = 536.1	N-{1-[(1-benzyl-4-ethylazetidin-2-yl)methyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
346		M+1 = 518.2	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[1-({[(1-hydroxycyclobutyl)methyl]amino}carbonyl)propyl]-1H-imidazol-4-yl}-L-norvalinamide
347		M+1 = 432	N-{1-[(4-benzylmorpholin-3-yl)methyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide

Ex	Structure	MS or NMR data	IUPACNAME
348		M+1 = 502	N-(1-{[4-(cyclopropylmethyl)morpholin-3-yl]methyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
349		M+1 = 446.0	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{1-[(dimethylamino)methyl]cyclopropyl}-1H-imidazol-4-yl)-L-norvalinamide
350		M+1 = 538	N-{1-[(4-benzylmorpholin-2-yl)methyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide
351		M+1 = 460.0	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{1-[(isopropylamino)methyl]cyclopropyl}-1H-imidazol-4-yl)-L-norvalinamide

Example 352

The following compounds are prepared utilizing the procedures described above:

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-ethoxy-propylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-fluoro-benzyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(3-fluoro-benzyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(4-methyl-benzyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(4-methoxy-benzyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(4-tert-butyl-benzyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-hydroxymethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-hydroxymethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-((R)-1-cyclohexyl-ethylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-((R)-1-cyclohexyl-ethylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(2,4-Difluoro-phenyl)-2-hydroxy-ethylamino]-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,4-Difluoro-phenyl)-2-hydroxy-ethylamino]-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1,1-dimethyl-2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1,1-dimethyl-2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-((S)-1-phenyl-ethylamino)-butyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(3-methyl-oxetan-3-ylmethyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(3-methyl-oxetan-3-ylmethyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-2-hydroxy-ethylamino]-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(2,4-Difluoro-phenyl)-2-hydroxy-ethylamino]-pentanoic acid {1-[2-((2R,6S)-2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(octahydro-pyrazino[1,2-a]azepin-2-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-([1,4]dioxan-2-ylmethyl-methyl-amino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(2-methoxy-1-methyl-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-oxo-piperazin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-benzylamino-ethyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-butoxy-propylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-((1R,2S)-2-hydroxymethyl-cyclohexylamino)-ethyl]-1H-imidazol-4-yl}-amide;

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[(4aS,8aS)-2-(octahydro-isoquinolin-2-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-isopropoxy-propylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(octahydro-isoquinolin-2-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3,4,5,6-tetrahydro-2H-[4,4']bipyridinyl-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(2-hydroxy-2-phenyl-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(indan-1-ylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(benzyl-methyl-amino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(indan-2-ylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3,4-dihydro-1#Hl-isoquinolin-2-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(2-propoxy-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-benzyl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-pyridin-2-yl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(methyl-pyridin-4-ylmethyl-amino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{2-[(2-methanesulfonyl-ethyl)-methyl-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(2-tert-butoxy-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-pyridin-4-yl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[(1-Hydroxy-cyclohexylmethyl)-amino]-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-[1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-2-phenyl-acetamide;

(S)-2-(Dicyclopropylmethyl-amino)-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-((R)-1-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(1-hydroxy-cyclohexylmethyl)-amino]-1,1-dimethyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-{1-[2-((2S,6R)-2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-phenyl-acetamide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(4-hydroxy-tetrahydro-pyran-4-ylmethyl)-amino]-1,1-dimethyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-dimethylaminomethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-piperidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-morpholin-4-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1-[((2R,6S)-2,6-dimethyl-morpholin-4-yl)methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1-[(2,2,2-trifluoro-ethylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1-[((R)-1-cyclohexyl-ethylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-hydroxymethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1-[(2,2-dimethyl-propylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[2-(2,2-dimethyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-phenyl-acetamide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(4-trifluoromethyl-phenyl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[1-(4-trifluoromethyl-phenyl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(2-methoxy-2-methyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1,1-dimethyl-2-[(3-methyl-oxetan-3-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(cyclohexylmethyl-amino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-indan-1-yl-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [(S)-1-((1S,2R)-2-hydroxy-indan-1-yl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [(R)-1-((1R,2S)-2-hydroxy-indan-1-yl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(2-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[1-(4-fluoro-phenyl)-2-hydroxy-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(3-methyl-benzylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(2-hydroxy-2-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(2-chloro-benzylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(3,4-dihydro-1H-isoquinolin-2-yl)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(indan-2-ylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(1-methoxymethyl-propylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(4-chloro-benzylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(2-methyl-benzylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(2-methoxy-ethylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{3-[(pyridin-3-ylmethyl)-amino]-propyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-((S)-1-p-tolyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(4-methoxy-benzylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(cyclopropylmethyl-amino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(4-methyl-benzylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(1-hydroxy-cyclohexylmethyl)-carbamoyl]-1,1-dimethyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(1,2,3,4-Tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1,1-dimethyl-2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(1-hydroxy-cyclohexylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(2,2,2-trifluoro-ethylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(2,2-dimethyl-propylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[((R)-1-cyclohexyl-ethylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-dimethylaminomethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-piperidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-morpholin-4-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[((2R,6S)-2,6-dimethyl-morpholin-4-yl)methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(4-hydroxy-tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(3-methyl-oxetan-3-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(1-hydroxy-cyclohexylmethyl)-amino]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1,1-dimethyl-3-[(pyridin-2-ylmethyl)-amino]-propyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(1-hydroxy-cyclohexylmethyl)-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-{[(2-Fluoro-3-trifluoromethyl-phenyl)methyl]-amino}-pentanoic acid {1-[2-((2R,6S)-2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-3-((S)-2,2,2-trifluoro-1-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-3-((R)-1-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(2-Trifluoromethyl-benzylamino)-pentanoic acid {1-[2-((2R,6S)-2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[(tetrahydro-pyran-4-ylmethyl)-carbamoyl]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(2-ethoxy-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {(R)-1-[(R)-1-(4-fluoro-phenyl)-2-hydroxy-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-hydroxymethyl-phenyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(2-ethoxy-ethylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[2-(2-ethoxy-ethylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-propionamide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-{1-[2-(2,2-dimethyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-phenyl-acetamide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-methyl-1-(2-methyl-benzylcarbamoyl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(2-methoxy-1-methyl-ethylcarbamoyl)-1-methyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {(S)-1-[2-(2,2-dimethyl-propylamino)-1-phenyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(3-benzylamino-propyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(2,2-dimethyl-propylamino)-methyl]-phenyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {(S)-1-[2-(2,2-dimethyl-propylamino)-1-phenyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(2-hydroxy-butylamino)-methyl]-phenyl}-1H-imidazol-4-yl)-amide;

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-{1-[2-(2,2-dimethyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-pyridin-3-yl-acetamide;

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-{1-[2-(2,2-dimethyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-(4-fluoro-phenyl)-acetamide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-methyl-1-(methyl-phenethyl-carbamoyl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(1,3-dihydro-isobenzofuran-5-ylcarbamoyl)-1-methyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(indan-1-ylcarbamoyl)-1-methyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-2-oxo-2-(3-pyridin-4-yl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[2-(3-fluoro-phenyl)-ethylcarbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-indan-1-yl-isobutyramide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(3-cyano-piperidin-1-yl)-1,1-dimethyl-2-oxo-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[methyl-(tetrahydro-pyran-2-ylmethyl)-carbamoyl]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[ethyl-(2-pyrazol-1-yl-ethyl)-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-2-oxo-2-(2-phenyl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[1,1-dimethyl-2-oxo-2-(3-pyridin-4-yl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-propionamide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(furan-2-ylmethyl)-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[3-(acetyl-methyl-amino)-pyrrolidin-1-yl]-1,1-dimethyl-2-oxo-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-methyl-1-((3R,4S)-4-methylsulfanyl-tetrahydro-furan-3-ylcarbamoyl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(4-acetyl-[1,4]diazepan-1-yl)-1,1-dimethyl-2-oxo-ethyl]-1H-imidazol-4-yl}-amide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-[2-(3-fluoro-phenyl)-ethyl]-isobutyramide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[1-(1-methyl-1H-pyrazol-4-yl)-ethylcarbamoyl]-ethyl}-1H-imidazol-4-yl)-amide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-methyl-N-phenethyl-isobutyramide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(3-methoxy-propylcarbamoyl)-1-methyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[(3-methyl-[1,2,4]oxadiazol-5-ylmethyl)-carbamoyl]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(2-cyano-ethyl)-methyl-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-ethyl-N-(2-pyrazol-1-yl-ethyl)-isobutyramide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-2-(3-methyl-5,6-dihydro-8H-[1,2,4]triazolo[4,3-a]pyrazin-7-yl)-2-oxo-ethyl]-1H-Imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[methyl-(1-methyl-1H-imidazol-2-ylmethyl)-carbamoyl]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[2-(4-hydroxymethyl-4-methyl-piperidin-1-yl)-1,1-dimethyl-2-oxo-ethyl]-1H-imidazol-4-yl}-propionamide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(4-methyl-benzyl)-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(1,3-dihydro-isobenzofuran-5-yl)-isobutyramide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[1,1-dimethyl-2-oxo-2-(2-phenyl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-propionamide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(2-diethylamino-ethyl)-methyl-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-N-{1-[2-(3-Cyano-piperidin-1-yl)-1,1-dimethyl-2-oxo-ethyl]-1H-imidazol-4-yl}-2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionamide;

(S)-N-(1-{2-[3-(Acetyl-methyl-amino)-pyrrolidin-1-yl]-1,1-dimethyl-2-oxo-ethyl}-1H-imidazol-4-yl)-2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionamide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-((1R,2S)-2-hydroxymethyl-cyclohexyl)-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(3-methyl-[1,2,4]oxadiazol-5-ylmethyl)-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-((S)-2-methoxy-1-methyl-ethyl)-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(3-methoxy-propyl)-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-[1-(1-methyl-1H-pyrazol-4-yl)-ethyl]-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(3-imidazol-1-yl-propyl)-isobutyramide; and

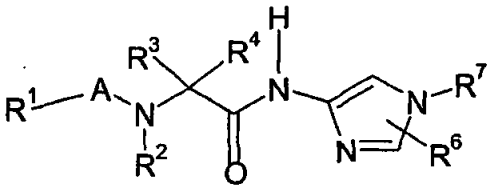
2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(3-morpholin-4-yl-propyl)-isobutyramide;

The invention described and claimed herein is not to be limited in scope by the specific embodiments herein disclosed, since these embodiments are intended as illustrations of several aspects of the invention. Any equivalent embodiments are intended to be within the scope of this invention. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description. Such modifications are also intended to fall within the scope of the appended claims.

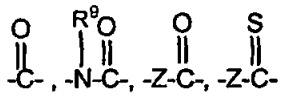
What is claimed is:

What is claimed is:

1. A compound of Formula I



I

wherein A is absent or is selected from  and SO_2;

Z is selected from $-CH_2$, $-CH(OH)$, $-CH(C_1-C_6$ alkyl), $-CH(C_1-C_6$ alkoxy), $-CH(NR^9R^{10})$, $-CH(CH_2(OH))$, $-CH(CH(C_1-C_4$ alkyl)(OH)) and $-CH(C(C_1-C_4$ alkyl)(C_1-C_4alkyl)(OH));

R^1 is selected from $-C_1-C_{20}$ alkyl, $-C_2-C_{20}$ alkenyl, $-C_2-C_{20}$ alkynyl, $-C_1-C_{20}$ alkoxy, $-C_2-C_{20}$ alkenoxy, $-C_1-C_{20}$ hydroxyalkyl, $-C_3-C_8$ cycloalkyl, benzo(C_3-C_8 cycloalkyl), benzo(C_3-C_8 heterocycloalkyl), $-C_4-C_8$ cycloalkenyl, $-(C_5-C_{11})$bi- or tricycloalkyl, benzo(C_5-C_{11})bi- or tricycloalkyl, (C_7-C_{11})bi- or tricycloalkenyl, (3-8 membered) heterocycloalkyl, $-C_6-C_{14}$ aryl and (5-14 membered) heteroaryl, wherein R^1 is optionally substituted by R^{1a};

wherein R^{1a} in each instance is independently selected from –OH, halo, $-C_1-C_6$ alkoxy, -CN, $-NO_2$, $-NR^9R^{10}$, $-C(=O)NR^9R^{10}$, $-C(=O)R^{11}$, $-C(=O)OR^{12}$, $-SO_2-NR^9R^{10}$, $-S(O)_n-R^{11}$, $-C_3-C_{15}$ cycloalkyl, $-C_4-C_{15}$ cycloalkenyl, $-(C_5-C_{11})$bi- or tricycloalkyl, $-(C_7-C_{11})$bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, $-C_6-C_{15}$ aryl, -(5-15 membered) heteroaryl, $-C_6-C_{15}$ aryloxy and -(5-15 membered) heteroaryloxy;

wherein said alkoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{1a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{1b};

wherein R^{1b} in each instance is independently selected from -OH, $-C_1-C_{12}$ alkyl, $-C_2-C_{12}$ alkenyl, $-C_2-C_{12}$ alkynyl, $-C_1-C_8$ alkoxy, $-C_1-C_{12}$ alkoxyalkyl $-C_1-C_{12}$ hydroxyalkyl, $-C_2-C_8$ alkenoxy, $-C_2-C_8$ alkynoxy, halo, -CN, $-NO_2$, $-NR^9R^{10}$, $-C(=O)NR^9R^{10}$, $-C(=O)R^{11}$, $-C(=O)OR^{12}$, $-SO_2-NR^9R^{10}$, $-S(O)_n-R^{11}$, $-C_3-C_{15}$ cycloalkyl, $-C_4-C_{15}$ cycloalkenyl, $-(C_5-C_{11})$bi- or tricycloalkyl, $-(C_7-C_{11})$bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, $-C_6-C_{15}$ aryl, -(5-15 membered) heteroaryl, $-C_6-C_{15}$ aryloxy and -(5-15 membered) heteroaryloxy;

R^2 is selected from H, $-C_1-C_8$ alkyl, $-C_2-C_8$ alkenyl, $-C_3-C_8$ cycloalkyl and $-C_3-C_8$ cycloalkenyl, wherein R^2 is optionally independently substituted with from one to three substituents independently selected from $-C_1-C_4$ alkyl optionally substituted with from one to

three halo atoms, -C_1-C_4 alkoxy optionally substituted with from one to three halo atoms, halo and -OH;

or R^1 and R^2 together with the A group when present and the nitrogen atom to which R^2 is attached, or R^1 and R^2 together with the nitrogen atom to which R^1 and R^2 are attached when A is absent, may optionally form a four to eight membered ring;

R^3 is selected from H, -C_1-C_6 alkyl, -C_2-C_6 alkenyl, -C_2-C_6 alkynyl, -C_3-C_8 cycloalkyl, -C_5-C_8 cycloalkenyl and (3-8 membered) heterocycloalkyl, -C_6-C_{14} aryl and -(5-14 membered) heteroaryl, wherein said alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, aryl or heteroaryl are each optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkoxy, halo, -OH, -S(C_1-C_4)alkyl, -C_1-C_4 alkyl -C(=O)OR^9, -SO_2R^9 and -(3-8 membered) heterocycloalkyl wherein said alkyl, alkoxy, and heterocyloalkyl may be further substituted by one to six halo;

R^4 is H,-C_1-C_8 alkyl or halo;

or R^3 and R^4 may together with the carbon atom to which they are attached optionally form a moiety selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, morpholino, piperidino, pyrrolidino, tetrahydrofuranyl and perhydro-2H-pyran, wherein said moiety formed by R^3 and R^4 is optionally substituted with from one to three substituents independently selected from -C_1-C_6 alkyl optionally substituted with from one to three halo atoms, -C_1-C_6 alkoxy optionally substituted with from one to three halo atoms, halo, -OH, -CN and allyl;

R^6 is selected from H, -C_1-C_6 alkyl, -C_2-C_6 alkylene, -C_1-C_6 alkoxy, halo, -CN, -C_3-C_{12} cycloalkyl ,-C_4-C_{12} cycloalkenyl (5-10 membered) heteroaryl and -C_6-C_{10} aryl, wherein said alkyl, alkylene and alkoxy of R^6 are each optionally independently substituted with from one to three substituents independently selected from halo and –CN, and wherein said cycloalkyl, cycloalkenyl, heteroaryl and aryl of R^6 are each optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkyl optionally substituted with from one to three halo atoms, -C_1-C_4 alkoxy optionally substituted with from one to three halo atoms, halo and –CN;

R^7 is -C_1-C_{20} alkyl substituted by -C_3-C_{12} cycloalkyl, -C_4-C_{12} cycloalkenyl, -(C_5-C_{20}) bi- or tricycloalkyl, -(C_7-C_{20})bi- or tricycloalkenyl, -(3-12 membered) heterocycloalkyl, -(7-20 membered) heterobi- or heterotricycloalkyl, -C_6-C_{14} aryl, benzo(C_3-C_8 heterocycloalkyl), -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy, wherein R^7 is independently substituted with from one to six substituents independently selected from R^{7a};

or R^7 is -C_3-C_{20} cycloalkyl, -C_4-C_{12} cycloalkenyl, -(C_5-C_{20}) bi- or tricycloalkyl, -(C_7-C_{20})bi- or tricycloalkenyl, -(3-12 membered) heterocycloalkyl, -(7-20 membered) heterobi- or heterotricycloalkyl, -C_6-C_{14} aryl, benzo(C_3-C_8 cycloalkyl), -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy substituted by at least one -C_1-C_{20} alkyl, wherein said cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, heterobi-

or heterotricycloalkyl, aryl, benzocycloalkyl, heteroaryl, aryloxy and heteroaryloxy is optionally independently substituted with from one to six substituents independently selected from R^{7a}; and wherein said alkyl is substituted by R^{7C};

wherein R^{7a} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl, -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy; wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenoxy, alkynoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{7a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{7b};

wherein R^{7b} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl, -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

wherein R^{7C} in each instance is independently selected from -C_1-C_6 alkoxy, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy; wherein said alkenoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{7c} are each optionally independently substituted with from one to six substituents independently selected from the group R^{7b};

or R^6 and R^7 may together with the carbon and nitrogen atoms to which they are respectively attached optionally form a -(5-8 membered) heterocycloalkyl ring, a -(5-8 membered) heterocycloalkenyl ring or a -(6-8 membered) heteroaryl ring, wherein said heterocycloalkyl, heterocycloalkenyl and heteroaryl rings are each optionally independently substituted with from one to three substituents independently selected from halo,-C_1-C_6 alkyl, optionally subsituted with from one to three halo atoms, -C_1-C_6 alkoxy optionally subsituted with from one to three halo atoms, -C_1-C_6 hydroxyalkyl, -OH, -$(CH_2)_{zero\text{-}10}NR^9R^{10}$, -$(CH_2)_{zero\text{-}10}$C(=O)$NR^9R^{10}$, -$SO_2NR^9R^{10}$ and -C_3-C_{12} cycloalkyl;

R^9 and R^{10} in each instance are each independently selected from H, -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl,

-C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy, wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenoxy, alkynoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^9 of R^{10} are each optionally independently substituted with from one to six substituents independently selected from the group R^{10a};

wherein R^{10a} in each instance is independently selected from –OH, halo, -C_1-C_{12} hydroxyalkyl, -C_1-C_6 alkoxy, -CN, -NO_2, -$NR^{11}R^{12}$, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{11}, -SO_2-$NR^{11}R^{12}$, -$S(O)_nR^{11}$, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy; wherein said alkoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{10a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{10b};

wherein R^{10b} in each instance is independently selected from -OH, halo; -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -$NR^{11}R^{12}$, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{11}, -SO_2-$NR^{11}R^{12}$, -$S(O)_nR^{11}$, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

or NR^9R^{10} may form a (4-20 membered) heterocycloalkyl, (5-18 membered) heterobi- or tricycloalkyl (5-18 membered) heterobi- or tricycloalkenyl, or -(5-15 membered) heteroaryl, wherein said heterocycloalkyl, heterobi- or tricycloalkyl, heterobi- or tricycloalkenyl or heteroaryl are optionally independently substituted with from one to six substituents independently selected from: -C_1-C_6 alkyl, -C_2-C_6 alkenyl, -C_2-C_6 alkenyl, -C_1-C_6 alkoxy, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, -C_1-C_6 hydroxyalkyl, -C_2-C_6 hydroxyalkenyl, -C_2-C_6 hydroxyalkenyl, halo, -OH, -CN, -NO_2, -$NR^{11}R^{12}$, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{11}, -$S(O)_nR^{11}$ and -$S(O)_n$-$NR^{11}R^{12}$;

R^{11} and R^{12} in each instance are each independently selected from H, -C_1-C_8 alkyl, -C_3-C_8 cycloalkyl, -C_4-C_8 cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, (3-8 membered) heterocycloalkyl,-C_6-C_{10} aryl and -(5-14 membered) heteroaryl, wherein said alkyl of R^{11} is optionally independently substituted with from one to three substituents independently selected from –OH, -CN and -C_3-C_8 cycloalkyl, and wherein each hydrogen atom of said alkyl is optionally independently replaced with a halo atom, and wherein said cylcoalkyl, cycloalkenyl, heterocycloalkyl, aryl and hetereoaryl of R^{11} are each optionally

independently substituted with from one to three substituents independently selected from halo, -C_1-C_8 alkyl optionally substituted with from one to three halo atoms, -OH, -CN and -C_3-C_8 cycloalkyl; and

n is in each instance an integer independently selected from zero, 1 and 2;

or a pharmaceutically acceptable salt thereof.

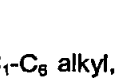
2. The compound of claim 1, wherein R^7 is a -C_4-C_8 cycloalkyl, -(4-10 membered) heterocycloalkyl, -C_6-C_{14} aryl or -(5-15 membered) heteroaryl substituted by a -C_1-C_4 alkyl and wherein said alkyl is further substituted by R^{7C}, wherein R^{7C} is $-NR^9R^{10}$.

3. The compound of claim 2, wherein R^9 is hydrogen or methyl, R^{10} is -C_1-C_8 alkyl or -C_4-C_8 cycloalkyl, wherein said alkyl or cycloalkyl of R^{10} is optionally substituted with from one to six substituents selected from R^{10a} wherein R^{10a} is selected from halo, -C_1-C_4 alkyl, -C_4-C_8 cycloalkyl, -(5-15 membered) heteroaryl or -C_1-C_4 hydroxyalkyl;

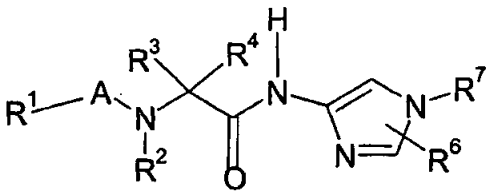
or $-NR^9R^{10}$ is a -(4-6 membered) heterocycloalkyl optionally substituted with from one to six substituents selected from halo, -C_1-C_4 alkyl or -C_1-C_4 hydroxyalkyl.

4. The compound of claim 1, wherein R^7 is a -C_1-C_8 alkyl substituted by a -C_4-C_8 cycloalkyl; -(C_5-C_{20}) bi- or tricycloalkyl, -(4-8 membered) heterocycloalkyl, -(7-12 membered) heterobi- or heterotricycloalkyl, -C_6-C_{14} aryl, benzo(C_3-C_8 cycloalkyl), -(5-15 membered) heteroaryl, wherein R^7 is optionally independently substituted with from one to six substituents independently selected from R^{7a}, wherein R^{7a} is $-NR^9R^{10}$, halo, -C_1-C_4 alkyl or -C_1-C_4 hydroxyalkyl.

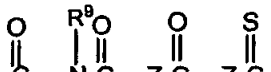
5. The compound of Claim 4, wherein R^7 is a -C_1-C_8 alkyl substituted by a -(4-8 membered) heterocycloalkyl or -C_6-C_{14} aryl, wherein R^7 is optionally independently substituted with from one to six substituents independently selected from R^{7a}, wherein R^{7a} is $-NR^9R^{10}$, halo, -OH, -C_1-C_4 alkyl or -C_1-C_4 hydroxyalkyl, wherein said alkyl or hydroxyalkyl is optional substituted with from one to six halo.

6. The compound of claim 1, wherein A is absent and R^1 is benzo(C_5-C_8 cycloalkyl) optionally substituted with from one to three substituents independently selected from -C_1-C_8 alkyl, halo and -OH; or A is  ; Z is $-CH_2$, –CH(OH) or –CH(-C_1-C_8 alkyl) and R^1 is -C_1-C_{10} alkyl, -C_6-C_{10} aryl or (6-10 membered) heteroaryl, wherein said alkyl, aryl and heteroaryl are optionally independently substituted with from one to three substituents independently selected from -C_1-C_8 alkyl, halo and -OH; R^2 is H or -C_1-C_8 alkyl; R^3 is H, $-CH_2CH_2SCH_3$, $-CH_2CH_2OCH_3$ or -C_1-C_8 alkyl; R^4 is H and R^8 is H or -C_1-C_8 alkyl.

7. A compound of Formula I



I

wherein A is absent or is selected from  and SO_2;

Z is selected from $-CH_2$, $-CH(OH)$, $-CH(C_1\text{-}C_6$ alkyl), $-CH(C_1\text{-}C_6$ alkoxy), $-CH(NR^9R^{10})$, $-CH(CH_2(OH))$, $-CH(CH(C_1\text{-}C_4$ alkyl)(OH)) and $-CH(C(C_1\text{-}C_4$ alkyl)($C_1\text{-}C_4$alkyl)(OH));

R^1 is selected from $-C_1\text{-}C_{20}$ alkyl, $-C_2\text{-}C_{20}$ alkenyl, $-C_2\text{-}C_{20}$ alkynyl, $-C_1\text{-}C_{20}$ alkoxy, $-C_2\text{-}C_{20}$ alkenoxy, $-C_1\text{-}C_{20}$ hydroxyalkyl, $-C_3\text{-}C_8$ cycloalkyl, benzo($C_3\text{-}C_8$ cycloalkyl), benzo($C_3\text{-}C_8$ heterocycloalkyl), $-C_4\text{-}C_8$ cycloalkenyl,, $-(C_5\text{-}C_{11})$bi- or tricycloalkyl, benzo($C_5\text{-}C_{11}$)bi- or tricycloalkyl, ($C_7\text{-}C_{11}$)bi- or tricycloalkenyl, -(3-8 membered) heterocycloalkyl, $-C_6\text{-}C_{14}$ aryl and -(5-14 membered) heteroaryl, wherein R^1 is optionally substituted by R^{1a};

wherein R^{1a} in each instance is independently selected from –OH, halo, $-C_1\text{-}C_6$ alkoxy, -CN, $-NO_2$, $-NR^9R^{10}$, $-C(=O)NR^9R^{10}$, $-C(=O)R^{11}$, $-C(=O)OR^{12}$, $-SO_2\text{-}NR^9R^{10}$, $-S(O)_n\text{-}R^{11}$, $-C_3\text{-}C_{15}$ cycloalkyl, $-C_4\text{-}C_{15}$ cycloalkenyl, $-(C_5\text{-}C_{11})$bi- or tricycloalkyl, $-(C_7\text{-}C_{11})$bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, $-C_6\text{-}C_{15}$ aryl, -(5-15 membered) heteroaryl, $-C_6\text{-}C_{15}$ aryloxy and -(5-15 membered) heteroaryloxy;

wherein said alkoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{1a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{1b};

wherein R^{1b} in each instance is independently selected from -OH, $-C_1\text{-}C_{12}$ alkyl, $-C_2\text{-}C_{12}$ alkenyl, $-C_2\text{-}C_{12}$ alkynyl, $-C_1\text{-}C_8$ alkoxy, $-C_1\text{-}C_{12}$ alkoxyalkyl $-C_1\text{-}C_{12}$ hydroxyalkyl, $-C_2\text{-}C_8$ alkenoxy, $-C_2\text{-}C_8$ alkynoxy, halo, -CN, $-NO_2$, $-NR^9R^{10}$, $-C(=O)NR^9R^{10}$, $-C(=O)R^{11}$, $-C(=O)OR^{12}$, $-SO_2\text{-}NR^9R^{10}$, $-S(O)_n\text{-}R^{11}$, $-C_3\text{-}C_{15}$ cycloalkyl, $-C_4\text{-}C_{15}$ cycloalkenyl, $-(C_5\text{-}C_{11})$bi- or tricycloalkyl, $-(C_7\text{-}C_{11})$bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, $-C_6\text{-}C_{15}$ aryl, -(5-15 membered) heteroaryl, $-C_6\text{-}C_{15}$ aryloxy and -(5-15 membered) heteroaryloxy;

R^2 is selected from H, $-C_1\text{-}C_6$ alkyl, $-C_2\text{-}C_8$ alkenyl, $-C_3\text{-}C_8$ cycloalkyl and $C_3\text{-}C_8$ cycloalkenyl, wherein R^2 is optionally independently substituted with from one to three substituents independently selected from $-C_1\text{-}C_4$ alkyl optionally substituted with from one to three halo atoms, $-C_1\text{-}C_4$ alkoxy optionally substituted with from one to three halo atoms, halo and -OH;

or R^1 and R^2 together with the A group when present and the nitrogen atom to which R^2 is attached, or R^1 and R^2 together with the nitrogen atom to which R^1 and R^2 are attached when A is absent, may optionally form a four to eight membered ring;

R^3 is selected from H, -C_1-C_6 alkyl, -C_2-C_6 alkenyl, -C_2-C_6 alkynyl, -C_3-C_6 cycloalkyl, -C_5-C_6 cycloalkenyl and (3-8 membered) heterocycloalkyl -C_6-C_{14} aryl and (5-14 membered) heteroaryl, wherein said alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl aryl or heteroaryl are each optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkoxy, halo, -OH, -S(C_1-C_4)alkyl -C_1-C_4 alkyl -C(=O)OR^9, -SO_2R^9 and -(3-8 membered) heterocycloalkyl wherein said alkyl, alkoxy, and heterocyloalkyl may be further substituted by one to six halo;

R^4 is H, -C_1-C_6 alkyl or halo;

or R^3 and R^4 may together with the carbon atom to which they are attached optionally form a moiety selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, morpholino, piperidino, pyrrolidino, tetrahydrofuranyl and perhydro-2H-pyran, wherein said moiety formed by R^3 and R^4 is optionally substituted with from one to three substituents independently selected from -C_1-C_6 alkyl optionally substituted with from one to three halo atoms, -C_1-C_6 alkoxy optionally substituted with from one to three halo atoms, halo, -OH, -CN and allyl;

R^6 is selected from H, -C_1-C_6 alkyl, -C_2-C_6 alkylene, -C_1-C_6 alkoxy, halo, -CN, -C_3-C_{12} cycloalkyl, -C_4-C_{12} cycloalkenyl -(5-10 membered) heteroaryl and -C_6-C_{10} aryl, wherein said alkyl, alkylene and alkoxy of R^6 are each optionally independently substituted with from one to three substituents independently selected from halo and –CN, and wherein said cycloalkyl, cycloalkenyl, heteroaryl and aryl of R^6 are each optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkyl optionally substituted with from one to three halo atoms, -C_1-C_4 alkoxy optionally substituted with from one to three halo atoms, halo and –CN;

R^7 is selected from -C_1-C_{20} alkyl, -C_1-C_{20} alkoxy, -C_1-C_{20} hydroxyalkyl, -C_3-C_{12} cycloalkyl, -C_4-C_{12} cycloalkenyl, -(C_5-C_{20}) bi- or tricycloalkyl, -(C_7-C_{20})bi- or tricycloalkenyl, (3-12 membered) heterocycloalkyl, -(7-20 membered) heterobi- or heterotricycloalkyl, -C_6-C_{14} aryl, -(5-15 membered) heteroaryl -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy, wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenoxy, alkynoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^7 are each independently substituted with from one to six substituents independently selected from the group R^{7a} or are each independently optionally substituted with from one to six substituents independently selected from the group R^{7d}

wherein R^{7a} in each instance is independently selected from -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C_3-C_{15} cycloalkyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered)

heteroaryloxy, wherein said alkyl, alkoxy, alkoxyalkyl, cycloalkyl, heterocycloalkyl, aryl heteroaryl, aryloxy, and heteroaryloxy of R^{7a} are each independently substituted by R^{7b} ;

wherein R^{7d} in each instance is independently selected from: -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -SO_2-NR^9R^{10}, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, ;wherein said alkenyl, alkynyl, hydroxyalkyl, alkenoxy, alkynoxy, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, of $R^{7d}$are each optionally independently substituted with from one to six substituents independently selected from the group R^{7b};

wherein R^{7b} in each instance is independently selected from -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

or R^8 and R^7 may together with the carbon and nitrogen atoms to which they are respectively attached optionally form a (5-8 membered) heterocycloalkyl ring, a (5-8 membered) heterocycloalkenyl ring or a (6-8 membered) heteroaryl ring, wherein said heterocycloalkyl, heterocycloalkenyl and heteroaryl rings are each optionally independently substituted with from one to three substituents independently selected from halo, -C_1-C_6 alkyl, optionally subsituted with from one to three halo atoms, -C_1-C_6 alkoxy optionally subsituted with from one to three halo atoms, -C_1-C_6 hydroxyalkyl, -OH, -$(CH_2)_{zero\text{-}10}NR^9R^{10}$, -$(CH_2)_{zero\text{-}10}C(=O)NR^9R^{10}$, -$SO_2NR^9R^{10}$ and -C_3-C_{12} cycloalkyl;

R^9 and R^{10} in each instance are each independently selected from -H, -$C(=O)R^{13}$ or -C_1-C_{20} alkyl, wherein at least one of R^9 and R^{10} are -$C(=O)R^{13}$ or -C_1-C_{20} alkyl, and wherein each -C_1-C_{20} alkyl is substituted with R^{10a}

wherein R^{10a} in each instance is independently selected from -C_1-C_6 alkoxy, -CN, -NO_2, -$NR^{11}R^{11}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy; wherein said alkoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{10a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{10b}

wherein R^{10b} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_nR^{11}$, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or

tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy

or NR^9R^{10} may form a (4-20 membered) heterocycloalkyl, (5-18 membered) heterobi- or tricycloalkyl, (5-18 membered) heterobi- or tricycloalkenyl, or -(5-15 membered) heteroaryl, wherein said heterocycloalkyl, heterobi- or tricycloalkyl, heterobi- or tricycloalkenyl or heteroaryl are optionally independently substituted with from one to six substituents independently selected from -C_1-C_8 alkyl, -C_2-C_8 alkenyl, -C_2-C_8 alkenyl, -C_1-C_8 alkoxy, -C_2-C_8 alkenoxy, -C_2-C_8 alkynoxy, -C_1-C_8 hydroxyalkyl, -C_2-C_8 hydroxyalkenyl, -C_2-C_8 hydroxyalkenyl, halo, -OH, -CN, -NO_2, $-NR^{11}R^{12}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-S(O)_nR^{11}$ and $-S(O)_nNR^{11}R^{12}$;

R^{11} and R^{12} in each instance are each independently selected from H, -C_1-C_8 alkyl, -C_3-C_8 cycloalkyl, -C_4-C_8 cycloalkenyl, (C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, (3-8 membered) heterocycloalkyl, -C_6-C_{10} aryl and (5-14 membered) heteroaryl, wherein said alkyl of R^{11} and $R^{12}$is optionally independently substituted with from one to three substituents independently selected from –OH, -CN and -C_3-C_8 cycloalkyl, and wherein each hydrogen atom of said alkyl is optionally independently replaced with a halo atom, and wherein said cylcoalkyl, cycloalkenyl, heterocycloalkyl, aryl and hetereoaryl of R^{11} and R^{12} are each optionally independently substituted with from one to three substituents independently selected from halo, -C_1-C_8 alkyl optionally substituted with from one to three halo atoms, -OH, -CN and -C_3-C_8 cycloalkyl;

R^{13} is in each instance is independently selected from alkyl substituted by -C_1-C_{12} alkoxy, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy; wherein said alkoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{13} is optionally substituted by one to three substituents independently selected from halo, -C_1-C_8 alkyl optionally substituted with from one to three halo atoms, -OH, -CN and -C_3-C_8 cycloalkyl;

n is in each instance an integer independently selected from zero, 1 and 2;

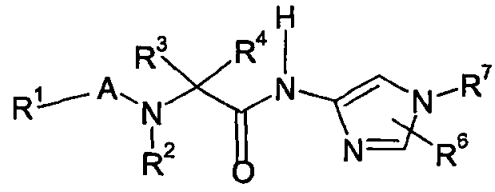
or a pharmaceutically acceptable salt thereof.

8. The compound of Claim 7, wherein R^7 is a -C_1-C_8 alkyl substituted by R^{7a}; R^{7a} is $-NR^9R^{10}$; R^9 is H or methyl; R^{10} is a -C_1-C_8 alkyl; R^{10a} is -C_1-C_8 alkoxy, –C_4-C_8 cycloalkyl, -(4-8 membered) heterocycloalkyl, -C_6-C_{15} aryl or -(5-15 membered) heteroaryl, wherein said alkoxy, cycloalkyl, heterocycloalkyl, aryl, heteroaryl of R^{10a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{10b}; wherein R^{10b} is halo, -OH, -C_1-C_4 alkyl or -C_1-C_4 hydroxyalkyl, wherein said alkyl or hydroxyalkyl of R^{10b} is optionally substituted by one to six halo.

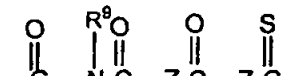
9. The compound of Claim 7, wherein R^7 is a -C_1-C_8 alkyl substituted by R^{7a}; R^{7a} is –C(=O)NR^9R^{10}; R^9 is H or methyl; R^{10} is a -C_1-C_8 alkyl; R^{10a} is -C_1-C_6 alkoxy, –C_4-C_8 cycloalkyl, -(4-8 membered) heterocycloalkyl, -C_6-C_{15} aryl or -(5-15 membered) heteroaryl, wherein said alkoxy, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{10a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{10b}; wherein R^{10b} is halo, -OH, -C_1-C_4 alkyl or -C_1-C_4 hydroxyalkyl, wherein said alkyl or hydroxyalkyl of R^{10b} is optionally substituted by one to six halo.

10 The compound of claim 7, wherein A is absent and R^1 is benzo(C_5-C_6 cycloalkyl) optionally substituted with from one to three substituents independently selected from -C_1-C_6 alkyl, halo and OH; or A is  ; Z is –CH_2, –CH(OH) or –CH(-C_1-C_8 alkyl) and R^1 is -C_1-C_{10} alkyl, -C_6-C_{10} aryl or (6-10 membered) heteroaryl, wherein said alkyl, aryl and heteroaryl are optionally independently substituted with from one to three substituents independently selected from -C_1-C_6 alkyl, halo and OH; R^2 is H or -C_1-C_6 alkyl; R^3 is H, –$CH_2CH_2SCH_3$, –$CH_2CH_2OCH_3$ or -C_1-C_6 alkyl; R^4 is H and R^6 is H or -C_1-C_6 alkyl.

11. A compound of Formula I



I

wherein A is absent or is selected from  , -Z-C-, -Z-C- and SO_2;

Z is selected from –CH_2, –CH(OH), –CH(-C_1-C_8 alkyl), –CH(-C_1-C_6 alkoxy), -CH(NR^9R^{10}), –CH(CH_2(OH)), –CH(CH(-C_1-C_4 alkyl)(OH)) and –CH(C(-C_1-C_4 alkyl)(-C_1-C_4alkyl)(OH));

R^1 is selected from -C_1-C_{20} alkyl, -C_2-C_{20} alkenyl, -C_2-C_{20} alkynyl, -C_1-C_{20} alkoxy, -C_2-C_{20} alkenoxy, -C_1-C_{20} hydroxyalkyl, -C_3-C_8 cycloalkyl, benzo(C_3-C_8 cycloalkyl), benzo(C_3-C_8 heterocycloalkyl), -C_4-C_8 cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, benzo(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(3-8 membered) heterocycloalkyl, -C_6-C_{14} aryl and -(5-14 membered) heteroaryl,wherein R1 is optionally substituted by R^{1a};

wherein R^{1a} in each instance is independently selected from –OH, halo, -C_1-C_6 alkoxy, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or

tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy,

wherein said alkoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{1a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{1b};

wherein R^{1b} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

R^2 is selected from H, -C_1-C_8 alkyl, -C_2-C_8 alkenyl, -C_3-C_8 cycloalkyl and -C_3-C_8 cycloalkenyl, wherein R^2 is optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkyl optionally substituted with from one to three halo atoms, -C_1-C_4 alkoxy optionally substituted with from one to three halo atoms, halo and -OH;

or R^1 and R^2 together with the A group when present and the nitrogen atom to which R^2 is attached, or R^1 and R^2 together with the nitrogen atom to which R^1 and R^2 are attached when A is absent, may optionally form a four to eight membered ring;

R^3 is selected from -C_6-C_{14} aryl and (5-14 membered) heteroaryl, wherein said aryl or heteroaryl are each optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkoxy, halo, -OH, -S(C_1-C_4)alkyl -C_1-C_4 alkyl -C(=O)OR^9, -SO_2R^9 and (3-8 membered) heterocycloalkyl wherein said alkyl, alkoxy, and heterocyloalkyl may be further substituted by one to six halo;

R^4 is H, -C_1-C_8 alkyl or halo;

or R^3 and R^4 may together with the carbon atom to which they are attached optionally form a moiety selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, morpholino, piperidino, pyrrolidino, tetrahydrofuranyl and perhydro-2H-pyran, wherein said moiety formed by R^3 and R^4 is optionally substituted with from one to three substituents independently selected from -C_1-C_6 alkyl optionally substituted with from one to three halo atoms, -C_1-C_6 alkoxy optionally substituted with from one to three halo atoms, halo, -OH, -CN and allyl;

R^6 is selected from H, -C_1-C_6 alkyl, -C_2-C_6 alkylene, -C_1-C_6 alkoxy, halo, -CN, -C_3-C_{12} cycloalkyl, -C_4-C_{12} cycloalkenyl (5-10 membered) heteroaryl and -C_6-C_{10} aryl, wherein said alkyl, alkylene and alkoxy of R^6 are each optionally independently substituted with from one to three substituents independently selected from halo and –CN, and wherein said cycloalkyl, cycloalkenyl, heteroaryl and aryl of R^6 are each optionally independently substituted with from

one to three substituents independently selected from -C_1-C_4 alkyl optionally substituted with from one to three halo atoms, -C_1-C_4 alkoxy optionally substituted with from one to three halo atoms, halo and –CN;

R^7 is selected from H, -C_1-C_{20} alkyl, -C_1-C_{20} alkoxy, -C_1-C_{20} hydroxyalkyl, -C_3-C_{12} cycloalkyl, -C_4-C_{12} cycloalkenyl, (C_5-C_{20}) bi- or tricycloalkyl, -(C_7-C_{20})bi- or tricycloalkenyl, (3-12 membered) heterocycloalkyl, -(7-20 membered) heterobi- or heterotricycloalkyl, -C_6-C_{14} aryl and -(5-15 membered) heteroaryl, wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenoxy, alkynoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^7 are each optionally independently substituted with from one to six substituents independently selected from the group R^{7a};

wherein R^{7a} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl, -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy; wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenoxy, alkynoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{7a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{7b};

wherein R^{7b} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{11}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

or R^6 and R^7 may together with the carbon and nitrogen atoms to which they are respectively attached optionally form a (5-8 membered) heterocycloalkyl ring, a (5-8 membered) heterocycloalkenyl ring or a (6-8 membered) heteroaryl ring, wherein said heterocycloalkyl, heterocycloalkenyl and heteroaryl rings are each optionally independently substituted with from one to three substituents independently selected from halo, -C_1-C_6 alkyl, optionally subsituted with from one to three halo atoms, -C_1-C_6 alkoxy optionally subsituted with from one to three halo atoms, -C_1-C_6 hydroxyalkyl, -OH, -$(CH_2)_{zero\text{-}10}NR^9R^{10}$, -$(CH_2)_{zero\text{-}10}$C(=O)$NR^9R^{10}$, -$SO_2NR^9R^{10}$ and -C_3-C_{12} cycloalkyl;

R^9 and R^{10} in each instance are each independently selected from H, -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-$NR^{10}R^{11}$, -

$S(O)_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy, wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenoxy, alkynoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^9 of R^{10} are each optionally independently substituted with from one to six substituents independently selected from the group R^{10a};

wherein R^{10a} in each instance is independently selected from –OH, halo, -C_1-C_6 alkoxy, -CN, -NO_2, -$NR^{11}R^{12}$, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy; wherein said alkoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{10a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{10b};

wherein R^{10b} in each instance is independently selected from -OH, halo; -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -$NR^{11}R^{12}$, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

or NR^9R^{10} may form may form a -(4-20 membered) heterocycloalkyl, -(5-18 membered) heterobi- or tricycloalkyl, -(5-18 membered) heterobi- or tricycloalkenyl, or -(5-15 membered) heteroaryl, wherein said heterocycloalkyl, heterobi- or tricycloalkyl, heterobi- or tricycloalkenyl or heteroaryl are optionally independently substituted with from one to six substituents independently selected from -C_1-C_6 alkyl, -C_2-C_6 alkenyl, -C_2-C_6 alkenyl, -C_1-C_6 alkoxy, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, -C_1-C_6 hydroxyalkyl, -C_2-C_6 hydroxyalkenyl, -C_2-C_6 hydroxyalkenyl, halo, -OH, -CN, -NO_2, -$NR^{11}R^{12}$, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{11}, -$S(O)_nR^{11}$ and -$S(O)_nNR^{11}R^{12}$;

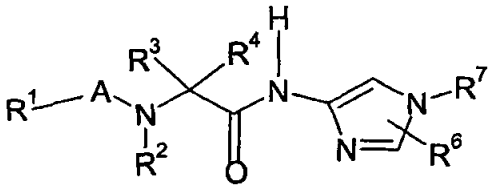
wherein R^{11} and R^{12} in each instance are each independently selected from H, -C_1-C_8 alkyl, -C_3-C_8 cycloalkyl, -C_4-C_8 cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(3-8 membered) heterocycloalkyl, -C_6-C_{10} aryl and -(5-14 membered) heteroaryl, wherein said alkyl of R^{11} is optionally independently substituted with from one to three substituents independently selected from –OH, -CN and -C_3-C_8 cycloalkyl, and wherein each hydrogen atom of said alkyl is optionally independently replaced with a halo atom, and wherein said cylcoalkyl, cycloalkenyl, heterocycloalkyl, aryl and hetereoaryl of R^{11} are each optionally independently substituted with from one to three substituents independently

selected from halo, -C_1-C_8 alkyl optionally substituted with from one to three halo atoms, -OH, -CN and -C_3-C_8 cycloalkyl; and

n is in each instance an integer independently selected from zero, 1 and 2;

or a pharmaceutically acceptable salt thereof.

12. A compound of Formula I



I

wherein A is absent;

R^1 is -C_1-C_{20} alkyl; wherein R^1 is independently substituted with from one to six substituents independently selected from R^{1A};

wherein R^{1a} in each instance is independently selected from -C_1-C_8 alkoxy, -CN, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

wherein said cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{1a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{1b};

wherein R^{1b} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_8 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_8 alkenoxy, -C_2-C_8 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

R^2 is selected from H, -C_1-C_8 alkyl, -C_2-C_8 alkenyl, -C_3-C_8 cycloalkyl and -C_3-C_8 cycloalkenyl, wherein R^2 is optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkyl optionally substituted with from one to three halo atoms, -C_1-C_4 alkoxy optionally substituted with from one to three halo atoms, halo and -OH;

R^3 is selected from H, -C_1-C_8 alkyl, -C_2-C_8 alkenyl, -C_2-C_8 alkynyl, -C_3-C_8 cycloalkyl, -C_5-C_8 cycloalkenyl and (3-8 membered) heterocycloalkyl, -C_6-C_{14} aryl and (5-14 membered) heteroaryl, wherein said alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl aryl or heteroaryl are each optionally independently substituted with from one to three substituents

independently selected from -C_1-C_4 alkoxy, halo, -OH, -S(C_1-C_4)alkyl -C_1-C_4alkyl -C(=O)OR^9, -SO_2R^9 and (3-8 membered) heterocycloalkyl wherein said alkyl, alkoxy, and heterocyloalkyl may be further substituted by one to six halo;

R^4 is H, -C_1-C_6 alkyl or halo;

or R^3 and R^4 may together with the carbon atom to which they are attached optionally form a moiety selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, morpholino, piperidino, pyrrolidino, tetrahydrofuranyl and perhydro-2H-pyran, wherein said moiety formed by R^3 and R^4 is optionally substituted with from one to three substituents independently selected from -C_1-C_6 alkyl optionally substituted with from one to three halo atoms, -C_1-C_6 alkoxy optionally substituted with from one to three halo atoms, halo, -OH, -CN and allyl;

R^6 is selected from H, -C_1-C_6 alkyl, -C_2-C_6 alkylene, -C_1-C_6 alkoxy, halo, -CN, -C_3-C_{12} cycloalkyl, -C_4-C_{12} cycloalkenyl (5-10 membered) heteroaryl and -C_6-C_{10} aryl, wherein said alkyl, alkylene and alkoxy of R^6 are each optionally independently substituted with from one to three substituents independently selected from halo and –CN, and wherein said cycloalkyl, cycloalkenyl, heteroaryl and aryl of R^6 are each optionally independently substituted with from one to three substituents independently selected from -C_1-C_4 alkyl optionally substituted with from one to three halo atoms, -C_1-C_4 alkoxy optionally substituted with from one to three halo atoms, halo and –CN;

R^7 is selected from H, -C_1-C_{20} alkyl, -C_1-C_{20} alkoxy, -C_1-C_{20} hydroxyalkyl, -C_3-C_{12} cycloalkyl, -C_4-C_{12} cycloalkenyl, -(C_5-C_{20}) bi- or tricycloalkyl, -(C_7-C_{20})bi- or tricycloalkenyl, (3-12 membered) heterocycloalkyl, (-7-20 membered) heterobi- or heterotricycloalkyl, -C_6-C_{14} aryl and (5-15 membered) heteroaryl, wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenoxy, alkynoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^7 are each optionally independently substituted with from one to six substituents independently selected from the group R^{7a};

wherein R^{7a} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl, -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy; wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenoxy, alkynoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{7a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{7b};

wherein R^{7b} in each instance is independently selected from -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6

alkenoxy, -C_2-C_8 alkynoxy, halo, -CN, -NO_2, -NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{11}, -SO_2-NR^9R^{10}, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

or R^8 and R^7 may together with the carbon and nitrogen atoms to which they are respectively attached optionally form a -(5-8 membered) heterocycloalkyl ring, a -(5-8 membered) heterocycloalkenyl ring or a -(6-8 membered) heteroaryl ring, wherein said heterocycloalkyl, heterocycloalkenyl and heteroaryl rings are each optionally independently substituted with from one to three substituents independently selected from halo, -C_1-C_6 alkyl, optionally subsituted with from one to three halo atoms, -C_1-C_6 alkoxy optionally subsituted with from one to three halo atoms, -C_1-C_6 hydroxyalkyl, -OH, -$(CH_2)_{zero\text{-}10}NR^9R^{10}$, -$(CH_2)_{zero\text{-}10}$C(=O)$NR^9R^{10}$, -$SO_2NR^9R^{10}$ and -C_3-C_{12} cycloalkyl;

R^9 and R^{10} in each instance are each independently selected from H, -OH, -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{11}, -SO_2-$NR^{11}R^{12}$, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy, wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenoxy, alkynoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^9 of R^{10} are each optionally independently substituted with from one to six substituents independently selected from the group R^{10a};

wherein R^{10a} in each instance is independently selected from –OH, Halo, -C_1-C_6 alkoxy, -CN, -NO_2, -$NR^{11}R^{12}$, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-$NR^{11}R^{12}$, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy; wherein said alkoxy, cycloalkyl, cycloalkenyl, bi- or tricycloalkyl, bi- or tricycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryloxy and heteroaryloxy of R^{10a} are each optionally independently substituted with from one to six substituents independently selected from the group R^{10b};

wherein R^{10b} in each instance is independently selected from -OH, halo; -C_1-C_{12} alkyl, -C_2-C_{12} alkenyl, -C_2-C_{12} alkynyl, -C_1-C_6 alkoxy, -C_1-C_{12} alkoxyalkyl -C_1-C_{12} hydroxyalkyl, -C_2-C_6 alkenoxy, -C_2-C_6 alkynoxy, halo, -CN, -NO_2, -$NR^{11}R^{12}$, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{11}, -SO_2-$NR^{11}R^{12}$, -S(O)$_n$-R^{11}, -C_3-C_{15} cycloalkyl, -C_4-C_{15} cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(4-20 membered) heterocycloalkyl, -C_6-C_{15} aryl, -(5-15 membered) heteroaryl, -C_6-C_{15} aryloxy and -(5-15 membered) heteroaryloxy;

or NR^9R^{10} may form a (4-20 membered) heterocycloalkyl, (5-18 membered) heterobi- or tricycloalkyl (5-18 membered) heterobi- or tricycloalkenyl, or -(5-15 membered) heteroaryl, wherein said a heterocycloalkyl, heterobi- or tricycloalkyl, heterobi- or tricycloalkenyl or heteroaryl are optionally independently substituted with from one to six substituents independently selected from -C_1-C_8 alkyl, -C_2-C_8 alkenyl, -C_2-C_8 alkenyl, -C_1-C_8 alkoxy, -C_2-C_8 alkenoxy, -C_2-C_8 alkynoxy,-C_1-C_8 hydroxyalkyl,-C_2-C_8 hydroxyalkenyl,-C_2-C_8 hydroxyalkenyl, halo, -OH, -CN, -NO_2, -$NR^{11}R^{12}$, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{11}, -S(O)$_n R^{11}$ and -S(O)$_n NR^{11}R^{12}$;

R^{11} and R^{12} in each instance are each independently selected from H, -C_1-C_8 alkyl, -C_3-C_8 cycloalkyl,-C_4-C_8 cycloalkenyl, -(C_5-C_{11})bi- or tricycloalkyl, -(C_7-C_{11})bi- or tricycloalkenyl, -(3-8 membered) heterocycloalkyl, -C_6-C_{10} aryl and -(5-14 membered) heteroaryl, wherein said alkyl of R^{11} is optionally independently substituted with from one to three substituents independently selected from –OH, -CN and-C_3-C_8 cycloalkyl, and wherein each hydrogen atom of said alkyl is optionally independently replaced with a halo atom, and wherein said cycloalkyl, cycloalkenyl, heterocycloalkyl, aryl and hetereoaryl of R^{11} are each optionally independently substituted with from one to three substituents independently selected from halo,-C_1-C_8 alkyl optionally substituted with from one to three halo atoms, -OH, -CN and-C_3-C_8 cycloalkyl; and

n is in each instance an integer independently selected from zero, 1 and 2;

or a pharmaceutically acceptable salt thereof.

13. A compound selected from the group consisting of:

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-ethoxy-propylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(octahydro-pyrazino[1,2-a]azepin-2-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-([1,4]dioxan-2-ylmethyl-methyl-amino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(2-methoxy-1-methyl-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-oxo-piperazin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-benzylamino-ethyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-butoxy-propylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-((1R,2S)-2-hydroxymethyl-cyclohexylamino)-ethyl]-1H-imidazol-4-yl}-amide;

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[(4aS,8aS)-2-(octahydro-isoquinolin-2-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-isopropoxy-propylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(octahydro-isoquinolin-2-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3,4,5,6-tetrahydro-2H-[4,4']bipyridinyl-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(2-hydroxy-2-phenyl-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(indan-1-ylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(benzyl-methyl-amino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(indan-2-ylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3,4-dihydro-1#H!-isoquinolin-2-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(2-propoxy-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-benzyl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-pyridin-2-yl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(methyl-pyridin-4-ylmethyl-amino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{2-[(2-methanesulfonyl-ethyl)-methyl-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(2-tert-butoxy-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-pyridin-4-yl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-fluoro-benzyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(3-fluoro-benzyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(4-methyl-benzyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(4-methoxy-benzyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(4-tert-butyl-benzyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-dimethylaminomethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-piperidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-morpholin-4-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1-[((2R,6S)-2,6-dimethyl-morpholin-4-yl)methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1-[(2,2,2-trifluoro-ethylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1-[((R)-1-cyclohexyl-ethylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1-[(2,2-dimethyl-propylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(2,2,2-trifluoro-ethylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(2,2-dimethyl-propylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[((R)-1-cyclohexyl-ethylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-dimethylaminomethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-piperidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-morpholin-4-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[((2R,6S)-2,6-dimethyl-morpholin-4-yl)methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-((R)-1-cyclohexyl-ethylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1,1-dimethyl-2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(1-hydroxy-cyclohexylmethyl)-amino]-1,1-dimethyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(4-hydroxy-tetrahydro-pyran-4-ylmethyl)-amino]-1,1-dimethyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(2-methoxy-2-methyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1,1-dimethyl-2-[(3-methyl-oxetan-3-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(cyclohexylmethyl-amino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-((R)-1-cyclohexyl-ethylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1,1-dimethyl-2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-((S)-1-phenyl-ethylamino)-butyl]-1H-imidazol-4-yl}-amide;

(S)-2-(Dicyclopropylmethyl-amino)-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-hydroxymethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-hydroxymethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-hydroxymethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(2,4-Difluoro-phenyl)-2-hydroxy-ethylamino]-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,4-Difluoro-phenyl)-2-hydroxy-ethylamino]-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-2-hydroxy-ethylamino]-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(2,4-Difluoro-phenyl)-2-hydroxy-ethylamino]-pentanoic acid {1-[2-((2R,6S)-2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[(1-Hydroxy-cyclohexylmethyl)-amino]-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-((R)-1-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(3-methyl-benzylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(2-hydroxy-2-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(2-chloro-benzylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(3,4-dihydro-1H-isoquinolin-2-yl)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(indan-2-ylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(1-methoxymethyl-propylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(4-chloro-benzylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(2-methyl-benzylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(2-methoxy-ethylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{3-[(pyridin-3-ylmethyl)-amino]-propyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-((S)-1-p-tolyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(4-methoxy-benzylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(cyclopropylmethyl-amino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(4-methyl-benzylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-methyl-1-(methyl-phenethyl-carbamoyl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(1,3-dihydro-isobenzofuran-5-ylcarbamoyl)-1-methyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(indan-1-ylcarbamoyl)-1-methyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-2-oxo-2-(3-pyridin-4-yl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[2-(3-fluoro-phenyl)-ethylcarbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(3-cyano-piperidin-1-yl)-1,1-dimethyl-2-oxo-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[methyl-(tetrahydro-pyran-2-ylmethyl)-carbamoyl]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[ethyl-(2-pyrazol-1-yl-ethyl)-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-2-oxo-2-(2-phenyl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(furan-2-ylmethyl)-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[3-(acetyl-methyl-amino)-pyrrolidin-1-yl]-1,1-dimethyl-2-oxo-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-methyl-1-((3R,4S)-4-methylsulfanyl-tetrahydro-furan-3-ylcarbamoyl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(4-acetyl-[1,4]diazepan-1-yl)-1,1-dimethyl-2-oxo-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[1-(1-methyl-1H-pyrazol-4-yl)-ethylcarbamoyl]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(3-methoxy-propylcarbamoyl)-1-methyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[(3-methyl-[1,2,4]oxadiazol-5-ylmethyl)-carbamoyl]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(2-cyano-ethyl)-methyl-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-2-(3-methyl-5,6-dihydro-8H-[1,2,4]triazolo[4,3-a]pyrazin-7-yl)-2-oxo-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[methyl-(1-methyl-1H-imidazol-2-ylmethyl)-carbamoyl]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(2-diethylamino-ethyl)-methyl-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-indan-1-yl-isobutyramide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[1,1-dimethyl-2-oxo-2-(3-pyridin-4-yl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-propionamide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[2-(4-hydroxymethyl-4-methyl-piperidin-1-yl)-1,1-dimethyl-2-oxo-ethyl]-1H-imidazol-4-yl}-propionamide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-methyl-N-phenethyl-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-ethyl-N-(2-pyrazol-1-yl-ethyl)-isobutyramide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[2-(4-hydroxymethyl-4-methyl-piperidin-1-yl)-1,1-dimethyl-2-oxo-ethyl]-1H-imidazol-4-yl}-propionamide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(4-methyl-benzyl)-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(1,3-dihydro-isobenzofuran-5-yl)-isobutyramide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[1,1-dimethyl-2-oxo-2-(2-phenyl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-propionamide;

(S)-N-{1-[2-(3-Cyano-piperidin-1-yl)-1,1-dimethyl-2-oxo-ethyl]-1H-imidazol-4-yl}-2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionamide;

(S)-N-(1-{2-[3-(Acetyl-methyl-amino)-pyrrolidin-1-yl]-1,1-dimethyl-2-oxo-ethyl}-1H-imidazol-4-yl)-2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionamide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-((1R,2S)-2-hydroxymethyl-cyclohexyl)-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(3-methyl-[1,2,4]oxadiazol-5-ylmethyl)-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-((S)-2-methoxy-1-methyl-ethyl)-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(3-methoxy-propyl)-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-[1-(1-methyl-1H-pyrazol-4-yl)-ethyl]-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(3-imidazol-1-yl-propyl)-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(3-morpholin-4-yl-propyl)-isobutyramide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(3-methyl-oxetan-3-ylmethyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(3-methyl-oxetan-3-ylmethyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(4-trifluoromethyl-phenyl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[1-(4-trifluoromethyl-phenyl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(2-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-(1,2,3,4-Tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1,1-dimethyl-2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(2-ethoxy-ethylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[2-(2-ethoxy-ethylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-propionamide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(1-hydroxy-cyclohexylmethyl)-carbamoyl]-1,1-dimethyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(1-hydroxy-cyclohexylmethyl)-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[(tetrahydro-pyran-4-ylmethyl)-carbamoyl]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-methyl-1-(2-methyl-benzylcarbamoyl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(2-methoxy-1-methyl-ethylcarbamoyl)-1-methyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(1-hydroxy-cyclohexylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(4-hydroxy-tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(3-methyl-oxetan-3-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(1-hydroxy-cyclohexylmethyl)-amino]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(2-ethoxy-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(3-benzylamino-propyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1,1-dimethyl-3-[(pyridin-2-ylmethyl)-amino]-propyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-3-((S)-2,2,2-trifluoro-1-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-3-((R)-1-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(2-Trifluoromethyl-benzylamino)-pentanoic acid {1-[2-((2R,6S)-2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-{[(2-Fluoro-3-trifluoromethyl-phenyl)methyl]-amino}-pentanoic acid {1-[2-((2R,6S)-2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-[1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-2-phenyl-acetamide

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-{1-[2-((2S,6R)-2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-phenyl-acetamide

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[2-(2,2-dimethyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-phenyl-acetamide

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-indan-1-yl-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [(S)-1-((1S,2R)-2-hydroxy-indan-1-yl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [(R)-1-((1R,2S)-2-hydroxy-indan-1-yl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[1-(4-fluoro-phenyl)-2-hydroxy-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {(R)-1-[(R)-1-(4-fluoro-phenyl)-2-hydroxy-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-hydroxymethyl-phenyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-{1-[2-(2,2-dimethyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-phenyl-acetamide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {(S)-1-[2-(2,2-dimethyl-propylamino)-1-phenyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {(S)-1-[2-(2,2-dimethyl-propylamino)-1-phenyl-ethyl]-1H-imidazol-4-yl}-amide;

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-{1-[2-(2,2-dimethyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-(4-fluoro-phenyl)-acetamide;

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-{1-[2-(2,2-dimethyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-pyridin-3-yl-acetamide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(2,2-dimethyl-propylamino)-methyl]-phenyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(2-hydroxy-butylamino)-methyl]-phenyl}-1H-imidazol-4-yl)-amide; (S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-ethoxy-propylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-fluoro-benzyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(3-fluoro-benzyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(4-methyl-benzyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(4-methoxy-benzyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(4-tert-butyl-benzyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-hydroxymethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-hydroxymethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-((R)-1-cyclohexyl-ethylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-((R)-1-cyclohexyl-ethylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(2,4-Difluoro-phenyl)-2-hydroxy-ethylamino]-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,4-Difluoro-phenyl)-2-hydroxy-ethylamino]-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1,1-dimethyl-2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1,1-dimethyl-2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-((S)-1-phenyl-ethylamino)-butyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(3-methyl-oxetan-3-ylmethyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(3-methyl-oxetan-3-ylmethyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-2-hydroxy-ethylamino]-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(2,4-Difluoro-phenyl)-2-hydroxy-ethylamino]-pentanoic acid {1-[2-((2R,6S)-2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(octahydro-pyrazino[1,2-a]azepin-2-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-([1,4]dioxan-2-ylmethyl-methyl-amino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(2-methoxy-1-methyl-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-oxo-piperazin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-benzylamino-ethyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-butoxy-propylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-((1R,2S)-2-hydroxymethyl-cyclohexylamino)-ethyl]-1H-imidazol-4-yl}-amide;

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[(4aS,8aS)-2-(octahydro-isoquinolin-2-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-isopropoxy-propylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(octahydro-isoquinolin-2-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3,4,5,6-tetrahydro-2H-[4,4']bipyridinyl-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(2-hydroxy-2-phenyl-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(indan-1-ylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(benzyl-methyl-amino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(indan-2-ylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3,4-dihydro-1#H!-isoquinolin-2-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(2-propoxy-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-benzyl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-pyridin-2-yl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(methyl-pyridin-4-ylmethyl-amino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{2-[(2-methanesulfonyl-ethyl)-methyl-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(2-tert-butoxy-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[2-(3-pyridin-4-yl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[(1-Hydroxy-cyclohexylmethyl)-amino]-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-[1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-2-phenyl-acetamide;

(S)-2-(Dicyclopropylmethyl-amino)-pentanoic acid [1-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-((R)-1-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(1-hydroxy-cyclohexylmethyl)-amino]-1,1-dimethyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-{1-[2-((2S,6R)-2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-phenyl-acetamide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(4-hydroxy-tetrahydro-pyran-4-ylmethyl)-amino]-1,1-dimethyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-dimethylaminomethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-piperidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(1-morpholin-4-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1-[((2R,6S)-2,6-dimethyl-morpholin-4-yl)methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1-[(2,2,2-trifluoro-ethylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1-[((R)-1-cyclohexyl-ethylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-hydroxymethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-(5,7-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-{1-[(2,2-dimethyl-propylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[2-(2,2-dimethyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-phenyl-acetamide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(4-trifluoromethyl-phenyl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[1-(4-trifluoromethyl-phenyl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(2-methoxy-2-methyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1,1-dimethyl-2-[(3-methyl-oxetan-3-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(cyclohexylmethyl-amino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid (1-indan-1-yl-1H-imidazol-4-yl)-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [(S)-1-((1S,2R)-2-hydroxy-indan-1-yl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [(R)-1-((1R,2S)-2-hydroxy-indan-1-yl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(2-pyrrolidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {1-[1-(4-fluoro-phenyl)-2-hydroxy-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(3-methyl-benzylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(2-hydroxy-2-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(2-chloro-benzylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(3,4-dihydro-1H-isoquinolin-2-yl)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(indan-2-ylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(1-methoxymethyl-propylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(4-chloro-benzylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(2-methyl-benzylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(2-methoxy-ethylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{3-[(pyridin-3-ylmethyl)-amino]-propyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-((S)-1-p-tolyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(4-methoxy-benzylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(cyclopropylmethyl-amino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[3-(4-methyl-benzylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(1-hydroxy-cyclohexylmethyl)-carbamoyl]-1,1-dimethyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(1,2,3,4-Tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1,1-dimethyl-2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(1-hydroxy-cyclohexylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(2,2,2-trifluoro-ethylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(2,2-dimethyl-propylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[((R)-1-cyclohexyl-ethylamino)-methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-dimethylaminomethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-piperidin-1-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(1-morpholin-4-ylmethyl-cyclobutyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[((2R,6S)-2,6-dimethyl-morpholin-4-yl)methyl]-cyclobutyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(4-hydroxy-tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(tetrahydro-pyran-4-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(3-methyl-oxetan-3-ylmethyl)-amino]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(1-hydroxy-cyclohexylmethyl)-amino]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1,1-dimethyl-3-[(pyridin-2-ylmethyl)-amino]-propyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(1-hydroxy-cyclohexylmethyl)-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-{[(2-Fluoro-3-trifluoromethyl-phenyl)methyl]-amino}-pentanoic acid {1-[2-((2R,6S)-2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-3-((S)-2,2,2-trifluoro-1-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-3-((R)-1-phenyl-ethylamino)-propyl]-1H-imidazol-4-yl}-amide;

(S)-2-(2-Trifluoromethyl-benzylamino)-pentanoic acid {1-[2-((2R,6S)-2,6-dimethyl-morpholin-4-yl)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[(tetrahydro-pyran-4-ylmethyl)-carbamoyl]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(2-ethoxy-ethylamino)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid {(R)-1-[(R)-1-(4-fluoro-phenyl)-2-hydroxy-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-pentanoic acid [1-(2-hydroxymethyl-phenyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(2-ethoxy-ethylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[2-(2-ethoxy-ethylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-propionamide;

(S)-2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-{1-[2-(2,2-dimethyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-phenyl-acetamide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-methyl-1-(2-methyl-benzylcarbamoyl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(2-methoxy-1-methyl-ethylcarbamoyl)-1-methyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {(S)-1-[2-(2,2-dimethyl-propylamino)-1-phenyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid [1-(3-benzylamino-propyl)-1H-imidazol-4-yl]-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(2,2-dimethyl-propylamino)-methyl]-phenyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {(S)-1-[2-(2,2-dimethyl-propylamino)-1-phenyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[(2-hydroxy-butylamino)-methyl]-phenyl}-1H-imidazol-4-yl)-amide;

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-{1-[2-(2,2-dimethyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-pyridin-3-yl-acetamide;

2-[2-(3,5-Difluoro-phenyl)-acetylamino]-N-{1-[2-(2,2-dimethyl-propylamino)-1,1-dimethyl-ethyl]-1H-imidazol-4-yl}-2-(4-fluoro-phenyl)-acetamide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-methyl-1-(methyl-phenethyl-carbamoyl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(1,3-dihydro-isobenzofuran-5-ylcarbamoyl)-1-methyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(indan-1-ylcarbamoyl)-1-methyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-2-oxo-2-(3-pyridin-4-yl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[2-(3-fluoro-phenyl)-ethylcarbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-indan-1-yl-isobutyramide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(3-cyano-piperidin-1-yl)-1,1-dimethyl-2-oxo-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[methyl-(tetrahydro-pyran-2-ylmethyl)-carbamoyl]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[ethyl-(2-pyrazol-1-yl-ethyl)-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-2-oxo-2-(2-phenyl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[1,1-dimethyl-2-oxo-2-(3-pyridin-4-yl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-propionamide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(furan-2-ylmethyl)-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{2-[3-(acetyl-methyl-amino)-pyrrolidin-1-yl]-1,1-dimethyl-2-oxo-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-methyl-1-((3R,4S)-4-methylsulfanyl-tetrahydro-furan-3-ylcarbamoyl)-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[2-(4-acetyl-[1,4]diazepan-1-yl)-1,1-dimethyl-2-oxo-ethyl]-1H-imidazol-4-yl}-amide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-[2-(3-fluoro-phenyl)-ethyl]-isobutyramide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[1-(1-methyl-1H-pyrazol-4-yl)-ethylcarbamoyl]-ethyl}-1H-imidazol-4-yl)-amide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-methyl-N-phenethyl-isobutyramide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1-(3-methoxy-propylcarbamoyl)-1-methyl-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[(3-methyl-[1,2,4]oxadiazol-5-ylmethyl)-carbamoyl]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(2-cyano-ethyl)-methyl-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-ethyl-N-(2-pyrazol-1-yl-ethyl)-isobutyramide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid {1-[1,1-dimethyl-2-(3-methyl-5,6-dihydro-8H-[1,2,4]triazolo[4,3-a]pyrazin-7-yl)-2-oxo-ethyl]-1H-imidazol-4-yl}-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-methyl-1-[methyl-(1-methyl-1H-imidazol-2-ylmethyl)-carbamoyl]-ethyl}-1H-imidazol-4-yl)-amide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[2-(4-hydroxymethyl-4-methyl-piperidin-1-yl)-1,1-dimethyl-2-oxo-ethyl]-1H-imidazol-4-yl}-propionamide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(4-methyl-benzyl)-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(1,3-dihydro-isobenzofuran-5-yl)-isobutyramide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-N-{1-[1,1-dimethyl-2-oxo-2-(2-phenyl-pyrrolidin-1-yl)-ethyl]-1H-imidazol-4-yl}-propionamide;

(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-pentanoic acid (1-{1-[(2-diethylamino-ethyl)-methyl-carbamoyl]-1-methyl-ethyl}-1H-imidazol-4-yl)-amide;

(S)-N-{1-[2-(3-Cyano-piperidin-1-yl)-1,1-dimethyl-2-oxo-ethyl]-1H-imidazol-4-yl}-2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionamide;

(S)-N-(1-{2-[3-(Acetyl-methyl-amino)-pyrrolidin-1-yl]-1,1-dimethyl-2-oxo-ethyl}-1H-imidazol-4-yl)-2-(6,8-difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionamide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-((1R,2S)-2-hydroxymethyl-cyclohexyl)-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(3-methyl-[1,2,4]oxadiazol-5-ylmethyl)-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-((S)-2-methoxy-1-methyl-ethyl)-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(3-methoxy-propyl)-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-[1-(1-methyl-1H-pyrazol-4-yl)-ethyl]-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(3-imidazol-1-yl-propyl)-isobutyramide;

2-{4-[(S)-2-(6,8-Difluoro-1,2,3,4-tetrahydro-naphthalen-2-ylamino)-propionylamino]-imidazol-1-yl}-N-(3-morpholin-4-yl-propyl)-isobutyramide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(1-hydroxycyclohexyl)methyl]amino}-11-dimethylethyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(3,5-difluorophenyl)acetyl]-N-{1-[1-(piperidin-1-ylmethyl)cyclobutyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[1-(pyrrolidin-1-ylmethyl)cyclobutyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(3,5-difluorophenyl)acetyl]-N-[1-(1-{[(2,2-dimethylpropyl)amino]methyl}cyclobutyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(3,5-difluorophenyl)acetyl]-N-[1-(1-{[(2,2-dimethylpropyl)amino]methyl}cyclobutyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(1-{[(22-dimethylpropyl)amino]methyl}cyclobutyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{1,1-dimethyl-2-[(2-methylbenzyl)amino]-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{1-methyl-2-[(tetrahydro-2H-pyran-4-ylmethyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(3-methoxypropyl)amino]-1,1-dimethyl-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2-hydroxybutyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide;

tert-butyl 3-{[4-({N-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalyl}amino)-1H-imidazol-1-yl]methyl}azetidine-1-carboxylate;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{[1-(2,2-dimethylpropyl)azetidin-3-yl]methyl}-1H-imidazol-4-yl)-L-norvalinamide;

2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-N-(2,2-dimethylpropyl)-2-methylpropanamide;

N-(2-chlorobenzyl)-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methylpropanamide;

2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-N-(2,3-dihydro-1H-inden-1-yl)-2-methylpropanamide;

N-[(1R)-1-cyclohexylethyl]-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methylpropanamide;

(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-N-{1-[11-dimethyl-2-(3-methylpiperidin-1-yl)-2-oxoethyl]-1H-imidazol-4-yl}-2-phenylacetamide;

2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methyl-N-(2-methylcyclohexyl)propanamide;

(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-N-{1-[1,1-dimethyl-2-(2-methylpiperidin-1-yl)-2-oxoethyl]-1H-imidazol-4-yl}-2-phenylacetamide;

(2S)-N-(1-{2-[(1R, 4S)-2-azabicyclo[2.2.1]hept-2-yl]-11-dimethyl-2-oxoethyl}-1H-imidazol-4-yl)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetamide;

2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methyl-N-(tetrahydro-2H-pyran-4-yl)propanamide;

(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-N-{1-[1,1-dimethyl-2-oxo-2-(3-phenylpyrrolidin-1-yl)ethyl]-1H-imidazol-4-yl}-2-phenylacetamide;

N-(3,4-difluorobenzyl)-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methylpropanamide;

(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-N-[1-(1,1-dimethyl-2-oxo-2-pyrrolidin-1-ylethyl)-1H-imidazol-4-yl]-2-phenylacetamide;

2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-N-(2,2-dimethylpropyl)-2-methylpropanamide;

N-cyclohexyl-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methylpropanamide;

2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methyl-N-(2-methylbenzyl)propanamide;

(2S)-N-(1-{2-[(1S5R)-6-azabicyclo[3.2.1]oct-6-yl]-11-dimethyl-2-oxoethyl}-1H-imidazol-4-yl)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetamide;

N-(2,4-difluorobenzyl)-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methylpropanamide;

(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-N-{1-[1,1-dimethyl-2-oxo-2-(3-pyridin-4-ylpyrrolidin-1-yl)ethyl]-1H-imidazol-4-yl}-2-phenylacetamide;

2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methyl-N-(4-methylcyclohexyl)propanamide;

2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)amino]-2-phenylacetyl}amino)-1H-imidazol-1-yl]-2-methyl-N-(3,3,5,5-tetramethylcyclohexyl)propanamide;

N-2-(6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl)-N-(1-{1,1-dimethyl-2-[(2-methylbenzyl)amino]-2-oxoethyl}-1H-imidazol-4-yl)-O-methyl-L-serinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{[1-(2,2-dimethylpropyl)pyrrolidin-2-yl]methyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{[1-(2,2-dimethylpropanoyl)pyrrolidin-2-yl]methyl}-1H-imidazol-4-yl)-L-norvalinamide;

(2S)-2-{[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]amino}-N-{1-[1-(2,2-dimethylpropyl)-2-oxopiperidin-3-yl]-1H-imidazol-4-yl}pentanamide

(2S)-N-[1-(1-benzyl-2-oxopiperidin-3-yl)-1H-imidazol-4-yl]-2-{[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]amino}pentanamide

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{[(2S)-1-(2,2-dimethylpropyl)azetidin-2-yl]methyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-({(2S)-1-[(2S)-2-hydroxybutyl]azetidin-2-yl}methyl)-1H-imidazol-4-yl]-L-norvalinamide;

tert-butyl 3-{[4-({N-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalyl}amino)-1H-imidazol-1-yl]methyl}-3-hydroxyazetidine-1-carboxylate

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{[1-(2,2-dimethylpropyl)-3-hydroxyazetidin-3-yl]methyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-{1-[(3S,4R)-1-benzyl-4-{2-[(2,2-dimethylpropyl)amino]ethyl}pyrrolidin-3-yl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2,2-dimethylpropyl)amino]methyl}-45-difluorophenyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-{1-[2-({3-[acetyl(methyl)amino]pyrrolidin-1-yl}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-{1-[2-({[(1R,2R)-2-(benzyloxy)cyclopentyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-(1-{2-[(4-acetyl-1,4-diazepan-1-yl)methyl]phenyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(3-hydroxypiperidin-1-yl)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1-ethylpiperidin-3-yl)methyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-{1-[2-({[(3R)-1-acetylpyrrolidin-3-yl]amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(4-ethylpiperazin-1-yl)methyl]phenyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1S,2R)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-(morpholin-4-ylmethyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2-morpholin-4-ylethyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(2-oxo-1,3-oxazinan-3-yl)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-(1-{2-[(bicyclo[1.1.1]pent-1-ylamino)methyl]phenyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2-propoxyethyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1-isobutyrylpiperidin-3-yl)methyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-{1-[2-({[(1R,2R)-2-(benzyloxy)cyclohexyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(dimethylamino)-2-oxoethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-(2,3-dihydro-1H-indol-1-ylmethyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-[1-(2-{[(2,4-difluorobenzyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(2-fluorophenoxy)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-{1-[2-({[2-(diethylamino)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(2-oxo-1,3-oxazolidin-3-yl)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(2-oxoimidazolidin-1-yl)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(3-methyl-1H-pyrazol-1-yl)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[1-(hydroxymethyl)pentyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2-isopropoxyethyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1R)-1-(hydroxymethyl)propyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-{1-[2-({[1-(4-chlorobenzyl)-2-hydroxyethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1,3-dimethylpyrrolidin-3-yl)methyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1,3-dimethylpyrrolidin-3-yl)methyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-(1-{2-[(4-acetylpiperazin-1-yl)methyl]phenyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-{1-[2-({[(1-tert-butyl-5-oxopyrrolidin-3-yl)methyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2-methoxyethyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2-ethoxyethyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(diisopropylamino)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[3-(1H-imidazol-1-yl)propyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1S)-1-(hydroxymethyl)-2,2-dimethylpropyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,23,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1S)-1-methyl-2-(methylamino)-2-oxoethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(dimethylamino)-1-methylethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(3-methyl-5,6-dihydro[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methyl]phenyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2-phenoxyethyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[methyl(1-methylpyrrolidin-3-yl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2,2,2-trifluoroethyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1S,2S)-1-(hydroxymethyl)-2-methylbutyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(2-oxopyrrolidin-1-yl)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(2,3-dihydro-1H-inden-2-ylamino)methyl]phenyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-{1-[2-({[2-(acetylamino)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[2-(dimethylamino)ethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-{1-[2-({[(1R)-1-benzyl-2-hydroxyethyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2-methylcyclohexyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1S)-1-(hydroxymethyl)-2-methylpropyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-(pyrrolidin-1-ylmethyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-{1-[2-({[3-(benzyloxy)-2-hydroxypropyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2-hydroxy-3-phenoxypropyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-(1-{2-[(tert-butylamino)methyl]phenyl}-1H-imidazol-4-yl)-N~2~-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(5-methylisoxazol-3-yl)methyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[({[(2R)-1-ethylpyrrolidin-2-yl]methyl}amino)methyl]phenyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-(1-{2-[({2-[butyl(methyl)amino]ethyl}amino)methyl]phenyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-(1-{2-[({2-[butyl(methyl)amino]ethyl}amino)methyl]phenyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(prop-2-yn-1-ylamino)methyl]phenyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(3-ethylisoxazol-5-yl)methyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-{1-[2-({[2-(diethylamino)ethyl](methyl)amino}methyl)phenyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-[1-(2-{[(2-tert-butoxyethyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[({[(2S)-1-ethylpyrrolidin-2-yl]methyl}amino)methyl]phenyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[1-(hydroxymethyl)butyl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(1,1-dioxidotetrahydro-3-thienyl)amino]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-[1-(2-{[(1R)-1-cyclohexylethyl]amino}-1,1-dimethyl-2-oxoethyl)-1H-imidazol-4-yl]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[1,1-dimethyl-2-oxo-2-(3-phenylpyrrolidin-1-yl)ethyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(1,1-dimethyl-2-{[(5-methyl-2-furyl)methyl]amino}-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[1-(methoxymethyl)propyl]amino}-1,1-dimethyl-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[1-(methoxymethyl)propyl]amino}-1,1-dimethyl-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-(1-{2-[(3,4-difluorobenzyl)amino]-1,1-dimethyl-2-oxoethyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(4-fluorobenzyl)amino]-1,1-dimethyl-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[2-(2-furyl)ethyl]amino}-1,1-dimethyl-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-(1-{2-[benzyl(ethyl)amino]-1,1-dimethyl-2-oxoethyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(1,1-dimethyl-2-{methyl[2-(1H-pyrazol-1-yl)ethyl]amino}-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-[1-(2-{[(1S)-1-cyclohexylethyl]amino}-1,1-dimethyl-2-oxoethyl)-1H-imidazol-4-yl]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-(1-{2-[(2,4-difluorobenzyl)amino]-1,1-dimethyl-2-oxoethyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{1,1-dimethyl-2-[methyl(2-pyridin-2-ylethyl)amino]-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(4-hydroxytetrahydro-2H-thiopyran-4-yl)methyl]amino}ethyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(2-methoxy-1-methylethyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(2-methoxy-1-methylethyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(3-ethoxypropyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(3-methoxypropyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(2-isopropoxyethyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(2-isopropoxyethyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2S)-tetrahydrofuran-2-ylmethyl]amino}ethyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2S)-tetrahydrofuran-2-ylmethyl]amino}ethyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-[1-(2-{[(1R)-1-cyclohexylethyl]amino}ethyl)-1H-imidazol-4-yl]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(3-isopropoxypropyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[2-(methylthio)ethyl]amino}ethyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(tetrahydro-2H-pyran-3-ylmethyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(2R)-tetrahydrofuran-2-ylmethyl]amino}ethyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(2-methoxyethyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-({1-[(2S)-2-hydroxybutyl]pyrrolidin-2-yl}methyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{[1-(2,2-dimethylpropyl)-3-hydroxypiperidin-3-yl]methyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-({1-[(2S)-2-hydroxybutyl]pyrrolidin-2-yl}methyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1,3-dimethylpyrrolidin-3-yl)methyl]amino}methyl)-4,5-difluorophenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-(1-{2-[({2-[butyl(methyl)amino]ethyl}amino)methyl]-45-difluorophenyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[1-(2,2-dimethylpropyl)-2-oxopyrrolidin-3-yl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{(1S)-2-[(3-methoxypropyl)amino]-1-methylethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[(1-hydroxycyclohexyl)methyl]amino}carbonyl)cyclobutyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-[1-(2-{[(3,4-difluorobenzyl)amino]carbonyl}cyclobutyl)-1H-imidazol-4-yl]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(2-methylbenzyl)amino]-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-oxo-2-[(tetrahydro-2H-pyran-2-ylmethyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-(1-{2-[(34-difluorobenzyl)amino]-2-oxoethyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-[1-(2-{[(1S)-1-cyclohexylethyl]amino}-2-oxoethyl)-1H-imidazol-4-yl]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(4-fluorobenzyl)amino]-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[2-(2-furyl)ethyl]amino}-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[methyl(2-pyridin-2-ylethyl)amino]-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(5-methyl-2-furyl)methyl]amino}-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-(1-{2-[(24-difluorobenzyl)amino]-2-oxoethyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-[1-(2-{[(1R)-1-cyclohexylethyl]amino}-2-oxoethyl)-1H-imidazol-4-yl]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-oxo-2-{[(2R)-tetrahydrofuran-2-ylmethyl]amino}ethyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-(1-{2-[benzyl(ethyl)amino]-2-oxoethyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[1-(tetrahydro-2H-pyran-4-ylmethyl)azetidin-3-yl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-({(2S)-1-[(2S)-2-hydroxypropyl]azetidin-2-yl}methyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[1-(trifluoroacetyl)pyrrolidin-3-yl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[1-(2,2,2-trifluoroethyl)pyrrolidin-3-yl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(3-methoxypropyl)amino]-1-methyl-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(tetrahydro-2H-pyran-4-ylamino)methyl]phenyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[4-(2,2,2-trifluoroethyl)piperazin-1-yl]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[4-(trifluoroacetyl)piperazin-1-yl]methyl}phenyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{(1S)-2-[(2-methoxyethyl)amino]-1-methylethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[(1S)-1-methyl-2-{methyl[(1-methyl-1H-pyrazol-4-yl)methyl]amino}ethyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[(1S)-1-methyl-2-(5-oxo-14-diazepan-1-yl)ethyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[(1S)-1-methyl-2-{methyl[2-(1H-pyrazol-4-yl)ethyl]amino}ethyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{(1S)-2-[(3-ethoxy-2-hydroxypropyl)amino]-1-methylethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{(1S)-2-[(2-methoxy-1-methylethyl)amino]-1-methylethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[(1S)-2-{[(1S)-2-methoxy-1-methylethyl]amino}-1-methylethyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[(1S)-1-methyl-2-{methyl[(1-methyl-1H-imidazol-2-yl)methyl]amino}ethyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[2-({[1-(trifluoroacetyl)piperidin-4-yl]amino}methyl)phenyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(1-hydroxycyclopentyl)methyl]amino}-1,1-dimethyl-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[4-(2-methoxyethoxy)piperidin-1-yl]-1,1-dimethyl-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(1-hydroxycyclobutyl)methyl]amino}-1,1-dimethyl-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(2-hydroxy-2-phenylpropyl)(methyl)amino]-1,1-dimethyl-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(1-hydroxycyclopentyl)methyl]amino}-1-methyl-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-[1-(2-{[(1-hydroxycyclobutyl)methyl]amino}-1-methyl-2-oxoethyl)-1H-imidazol-4-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[(2-hydroxy-2-phenylpropyl)(methyl)amino]-1-methyl-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{1-methyl-2-oxo-2-[(tetrahydro-1H-pyrrolizin-7a(5H)-ylmethyl)amino]ethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{2-[2-(2-hydroxyethyl)piperidin-1-yl]-1-methyl-2-oxoethyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[1-({[1-(methoxymethyl)propyl]amino}carbonyl)propyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[1-({[1-(methoxymethyl)propyl]amino}methyl)propyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[(1S,2S)-2-{[(2-morpholin-4-ylethyl)amino]carbonyl}cyclobutyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[(1R,2R)-2-({[1-(methoxymethyl)propyl]amino}carbonyl)cyclobutyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-{1-[(1-benzyl-4-ethylazetidin-2-yl)methyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-{1-[1-({[(1-hydroxycyclobutyl)methyl]amino}carbonyl)propyl]-1H-imidazol-4-yl}-L-norvalinamide;

N-{1-[(4-benzylmorpholin-3-yl)methyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-(1-{[4-(cyclopropylmethyl)morpholin-3-yl]methyl}-1H-imidazol-4-yl)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{1-[(dimethylamino)methyl]cyclopropyl}-1H-imidazol-4-yl)-L-norvalinamide;

N-{1-[(4-benzylmorpholin-2-yl)methyl]-1H-imidazol-4-yl}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-L-norvalinamide;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahydronaphthalen-2-yl]-N-(1-{1-[(isopropylamino)methyl]cyclopropyl}-1H-imidazol-4-yl)-L-norvalinamide;

and pharmaceutically acceptable salts thereof.

14. A pharmaceutical composition for treating a disease or condition selected from the group consisting of Alzheimer's disease, hereditary cerebral hemorrhage with amyloidosis, cerebral amyloid angiopathy, a prion-mediated disease, inclusion body myositis, stroke, multiple sclerosis, head trauma, mild cognitive impairment and Down's Syndrome in a mammal, comprising an amount of the compound according to claim 1 that is effective in inhibiting Aβ-peptide production or treating such disease or condition, and a pharmaceutically acceptable carrier.

15. A pharmaceutical composition for treating a disease or condition selected from the group consisting of Alzheimer's disease, hereditary cerebral hemorrhage with amyloidosis, cerebral amyloid angiopathy, a prion-mediated disease, inclusion body myositis, stroke, multiple sclerosis, head trauma, mild cognitive impairment and Down's Syndrome in a mammal, comprising an amount of the compound according to claim 7 that is effective in inhibiting Aβ-peptide production or treating such disease or condition, and a pharmaceutically acceptable carrier.

16. A method of treating a disease or condition selected from the group consisting of Alzheimer's disease, hereditary cerebral hemorrhage with amyloidosis, cerebral amyloid angiopathy, a prion-mediated disease, inclusion body myositis, stroke, multiple sclerosis, head trauma, mild cognitive impairment and Down's Syndrome in a mammal,

comprising administering to said mammal an amount of the compound according to claim 1 that is effective in inhibiting Aβ-production or treating such disease or condition.

17. A method of treating a disease or condition selected from the group consisting of Alzheimer's disease, hereditary cerebral hemorrhage with amyloidosis, cerebral amyloid angiopathy, a prion-mediated disease, inclusion body myositis, stroke, multiple sclerosis, head trauma, mild cognitive impairment and Down's Syndrome in a mammal, comprising administering to said mammal an amount of the compound according to claim 7 that is effective in inhibiting Aβ-production or treating such disease or condition.

18. A pharmaceutical composition for treating a disease or condition associated with the modulation of the Notch signaling pathway comprising the compound of Formula I according to claim 1, or their pharmaceutically acceptable salts.

19. A pharmaceutical composition for treating a disease or condition associated with the modulation of the Notch signaling pathway comprising the compound of Formula I according to claim 1, or their pharmaceutically acceptable salts.

PC33065A

COMPUESTOS DE IMIDAZOL PARA EL TRATAMIENTO DE TRASTORNOS NEUROLÓGICOS

Campo de la invención

La presente invención se refiere al tratamiento de trastornos neurodegenerativos y/o neurológicos, tal como enfermedad de Alzheimer, en mamíferos, incluyendo seres humanos. Esta invención también se refiere a la inhibición, en mamíferos, incluyendo seres humanos, de la producción de Aβ - péptidos que pueden contribuir a la formación de depósitos neurológicos de la proteína amiloide. Más particularmente, esta invención se refiere a compuestos de imidazol, composiciones farmacéuticas que comprenden tales compuestos y procedimientos de uso de tales compuestos, en concreto, para el tratamiento de trastornos neurodegenerativos y/o neurológicos, tales como enfermedad de Alzheimer, relacionados con la producción de Aβ - péptidos.

Antecedentes de la invención

La demencia se produce a partir de una amplia diversidad de procesos patológicos distintos. Los procesos patológicos más comunes que producen demencia son enfermedad de Alzheimer (AD), angiopatía amiloide cerebral (CAA) y enfermedades mediadas por priones. La AD afecta a casi la mitad de todas las personas que pasan la edad de 85 años, la parte que más rápidamente está creciendo de la población de Estados Unidos. Como tal, el número de pacientes de AD en los Estados Unidos se espera que se incremente entre aproximadamente 4 millones y aproximadamente 14 millones a mediados del próximo siglo.

El tratamiento de la AD típicamente es el apoyo proporcionado por un

miembro de la familia en misión de asistencia. Los ejercicios de memoria estimulados en base regular se ha mostrado que reducen, pero no detienen, la pérdida de memoria. Unos pocos fármacos, por ejemplo, Aricept ™, proporcionan tratamiento de la AD.

Un sello de la AD es la acumulación en el cerebro de depósitos insolubles extracelulares llamados placas amiloides y lesiones anormales dentro de las células neuronales llamadas marañas neurofibrilares. El incremento de la formación de las placas está asociado a un incremento de riesgo de la AD. De hecho la presencia de placas amiloides, junto con marañas neurofibrilares, es la base para la diagnosis patológica definitiva de la AD.

Los componentes principales de las placas amiloides son los Aβ - péptidos amiloides, también llamados Aβ - péptidos, que constan de varias proteínas incluyendo 38, 40, 42 ó 43 aminoácidos, denominadas $A\beta_{1-38}$, $A\beta_{1-40}$, $A\beta_{1-42}$ y $A\beta_{1-43}$ péptidos respectivamente. Los Aβ - péptidos se cree que producen la destrucción de las células nerviosas, en parte, debido a que son tóxicos para las neuronas *in vitro* e *in vivo*.

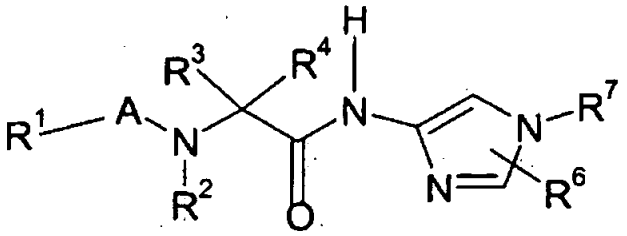
Los Aβ - péptidos se derivan de proteínas precursoras amiloides (proteínas APP) mayores, que constan de cuatro proteínas que contienen 695, 714, 751 ó 771 aminoácidos, denominadas APP_{695}, APP_{714}, APP_{751} y APP_{771} respectivamente. Las proteasas se cree que producen los Aβ - péptidos mediante la escisión de secuencias de aminoácidos específicas dentro de las diversas proteínas APP. Las proteasas se llaman "secretasas" debido a que los Aβ - péptidos que producen se secretan por las células en el entorno extracelular. Estas secretasas se denominan cada una según la (s) escisión (es) que realice (n) para producir los Aβ - péptidos. La secretasa que forma el

extremo amino terminal de los Aβ - péptidos se llama la beta - secretasa. La secretasa que forma el extremo carboxi terminal de los Aβ - péptidos se llama gamma - secretasa.

Esta invención se refiere a compuestos novedosos que inhiben la producción de Aβ - péptidos, a las composiciones farmacéuticas que comprenden tales compuestos, y a los procedimientos de uso de tales compuestos para tratar trastornos neurodegenerativos y/o neurológicos.

Resumen de la invención

La presente invención se refiere a los compuestos de la fórmula I



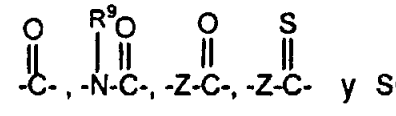
I

en la que R^1 , R^2 , R^3 , R^4 , R^6 , R^7 y A son como se define más adelante. Los compuestos de fórmula I tienen actividad inhibidora de la producción de Aβ - péptido. La invención también se refiere a composiciones farmacéuticas y procedimientos para tratar enfermedades y trastornos, por ejemplo, trastornos neurodegenerativos y/o neurológicos, por ejemplo enfermedad de Alzheimer, en un mamífero que comprende compuestos de fórmula I.

Descripción detallada de la invención

En una realización, la presente invención se refiere a compuestos de

fórmula I en la que A está ausente o se selecciona entre



Z se selecciona entre $-CH_2$, -CH(OH), -CH(alquilo C_1 - C_6), -CH(alcoxi C_1 - C_6), $-CH(NR^9R^{10})$, $-CH(CH_2(OH))$, -CH(CH(alquilo C_1 - C_4)(OH)) y -CH(C(alquilo C_1 - C_4)(alquilo C_1 - C_4)(OH));

R^1 se selecciona entre alquilo C_1 - C_{20}, alquenilo C_2 - C_{20}, alquinilo C_2 - C_{20}, alcoxi C_1 - C_{20}, alquenoxi C_2 - C_{20}, hidroxialquilo C_1 - C_{20}, cicloalquilo C_3 - C_8, benzo (cicloalquilo C_3 - C_8), benzo (heterocicloalquilo C_3 - C_8), cicloalquenilo C_4 - C_8, bi- o tricicloalquilo (C_5 - C_{11}), benzo bi- o tricicloalquilo (C_5 - C_{11}), bi- o tricicloalquenilo (C_7 - C_{11}), heterocicloalquilo de (entre 3 y 8 miembros), arilo C_6 - C_{14} y heteroarilo de (entre 5 y 14 miembros), en el que R^1 está opcionalmente sustituido con R^{1a};

en la que R^{1a} en cada caso se selecciona independientemente entre -OH, halo, -alcoxi C_1 - C_6, -CN, $-NO_2$, NR^9R^{10}, $-C(=O)NR^9R^{10}$, $-C(=O)R^{11}$, $-C(=O)OR^{12}$, $-SO_2-NR^9R^{10}$, $-S(O)_n-R^{11}$, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), - heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

en la que dicho alcoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{1a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{1b};

en la que R^{1b} se selecciona en cada caso independientemente entre -OH, - alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -

alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -NR^9R^{10}, -C-(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

R^2 se selecciona entre H, alquilo C_1 - C_6, alquenilo C_2 - C_6, cicloalquilo C_3 - C_8 y cicloalquenilo C_3 - C_8, en el que R^2 está sustituido opcional e independientemente con entre uno a tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, alcoxi C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, halo y -OH.

o R^1 y R^2 junto con el grupo A cuando está presente y el átomo de nitrógeno al que R^2 está unido, o R^1 y R^2 junto con el átomo de nitrógeno al que R^1 y R^2 están unidos cuando A está ausente, pueden opcionalmente formar un anillo de cuatro a ocho miembros;

R^3 se selecciona entre H, alquilo C_1 - C_6, alquenilo C_2 - C_6, alquinilo C_2 - C_6, cicloalquilo C_3 - C_6, cicloalquenilo C_5 - C_6 y heterocicloalquilo de (entre 3 y 8 miembros), -arilo C_6 - C_{14} y heteroarilo de (entre 5 y 14 miembros), en el que dicho alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquenilo, heterocicloalquilo, arilo o heteroarilo están cada uno de ellos opcional e independientemente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre alcoxi C_1 - C_4, halo, -OH, -S alquilo (C_1 - C_4), -alquilo (C_1 - C_4), -C(=O)OR^9, -SO_2R^9 y heterocicloalquilo de (entre 3 y 8 miembros) en el que dicho alquilo, alcoxi, y heterocicloalquilo puede estar adicionalmente

sustituido con uno a seis halo;

R^4 es H, alquilo C_1 - C_6 o halo;

o R^3 y R^4 pueden junto con el átomo de carbono al que están unidos opcionalmente formar un resto seleccionado entre ciclopropilo, ciclobutilo, ciclopentilo, ciclohexilo, morfolino, piperidino, pirrolidino, tetrahidrofuranilo y perhidro-2H-pirano, en el que dicho resto formado por R^3 y R^4 está opcionalmente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, alcoxi C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, halo, -OH, -CN y alilo;

R^6 se selecciona entre H, alquilo C_1 - C_6, alquileno C_2 - C_6, alcoxi C_1 - C_6, halo, -CN, cicloalquilo C_3 - C_{12}, cicloalquenilo C_4 - C_{12}, heteroarilo de (entre 5 y 10 miembros) y arilo C_6 - C_{10}, en el que dicho alquilo, alquileno y alcoxi de R^6 están cada uno de ellos opcional e independientemente sustituidos con entre uno a tres sustituyentes seleccionados independientemente entre halo y -CN, y en el que dicho cicloalquilo, cicloalquenilo, heteroarilo y arilo de R^6 están cada uno de ellos opcional e independientemente sustituidos con entre uno a tres sustituyentes seleccionados independientemente entre -alquilo C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, halo y -CN;

R^7 es alquilo C_1 - C_{20} sustituido con -cicloalquilo C_3 - C_{12}, cicloalquenilo C_4 - C_{12}, bi- o tricicloalquilo (C_5 - C_{20}), bi- o tricicloalquenilo (C_7 - C_{20}), heterocicloalquilo de (entre 3 y 12 miembros), heterobi- o heterotricicloalquilo de (entre 7 y 20 miembros), arilo C_6 - C_{14}, benzo (heterocicloalquilo C_3 - C_8), heteroarilo de (entre 5 y 15 miembros), -ariloxi C_6 - C_{15} y -heteroariloxi de (entre

5 y 15 miembros), en el que R^7 está independientemente sustituido con entre uno y seis sustituyentes seleccionados independientemente entre R^{7a};

o R^7 es -cicloalquilo C_3 - C_{20}, -cicloalquenilo C_4 - C_{12}, bi- o tricicloalquilo (C_5 - C_{20}), bi- o tricicloalquenilo (C_7 - C_{20}), -heterocicloalquilo de (entre 3 y 12 miembros), -heterobi o heterotricicloalquilo de (entre 7 y 20 miembros) , -arilo C_6 - C_{14}, benzo (cicloalquilo C_3 - C_8), heteroarilo de (entre 5 y 15 miembros), -ariloxi C_6 - C_{15} y -heteroariloxi de (entre 5 y 15 miembros) sustituido con al menos un -alquilo C_1 - C_{20}, en el que dichos cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, heterobi o heterotricicloalquilo, arilo, benzocicloalquilo, heteroarilo, ariloxi y heteroariloxi está opcional e independientemente sustituido con entre uno y seis sustituyentes seleccionados independientemente entre R^{7a}; en el que dicho alquilo está sustituido con R^{7c};

en la que R^{7a} en cada caso se selecciona independientemente entre -OH, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, $-NO_2$, $-NR^9R^{10}$, $-C(=O)NR^9R^{10}$, $-C(=O)R^{11}$, $-C(=O)OR^{12}$, $-SO_2-NR^9R^{10}$, $-S(O)_n-R^{11}$, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alquilo, alquenilo, alquinilo, alcoxi, alquenoxi, alquinoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{7a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados

independientemente entre el grupo R^{7b};

en la que R^{7b} en cada caso se selecciona independientemente entre -OH, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

en la que R^{7C} en cada caso se selecciona independientemente entre -alcoxi C_1 - C_6, -CN, -NO_2, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alquenoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{7c} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{7b};

o R^6 y R^7 pueden junto con los átomos de carbono y nitrógeno a los que están respectivamente unidos opcionalmente formar un anillo heterocicloalquilo de (entre 5 y 8 miembros), un anillo heterocicloalquenilo de (entre 5 y 8 miembros) o un anillo heteroarilo de (entre 6 y 8 miembros) , en el que dichos anillos heterocicloalquilo, heterocicloalquenilo y heteroarilo están opcional e independientemente sustituidos cada uno con entre uno a tres sustituyentes

seleccionados independientemente entre halo, -alquilo C_1 - C_6, opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, -hidroxialquilo C_1 - C_6, -OH, -$(CH_2)_{cero\text{ - }10}$ NR^9R^{10}, -$(CH_2)_{cero\text{ - }10}$ $C(=O)NR^9R^{10}$, -$SO_2NR^9R^{10}$ y cicloalquilo C_3 - C_{12};

R^9 y R^{10} se seleccionan en cada caso cada uno de ellos independientemente entre H, -OH, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6 -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alquilo, alquenilo, alquinilo, alcoxi, alquenoxi, alquinoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^9 y R^{10} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{10a};

en la que R^{10a} en cada caso se selecciona independientemente entre -OH, halo, -hidroxialquilo C_1 - C_{12}, -alcoxi C_1 - C_6, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, -cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alcoxi, cicloalquilo, cicloalquenilo, bi- o

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tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{10a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{10b};

en la que R^{10b} en cada caso se selecciona independientemente entre -OH, halo, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

o NR^9R^{10} puede formar un heterocicloalquilo de (entre 4 y 20 miembros), heterobi- o tricicloalquilo de (entre 5 y 18 miembros), heterobi- o tricicloalquenilo de (entre 5 y 18 miembros), o heteroarilo de (entre 5 y 15 miembros), en el que dicho heterocicloalquilo, heterobi- o tricicloalquilo, heterobi- o tricicloalquenilo o heteroarilo están opcionalmente e independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre alquilo C_1 - C_6, -alquenilo C_2 - C_6, -alquenilo C_2 - C_6, alcoxi C_1 - C_6, alquenoxi C_2 - C_6, alquinoxi C_2 - C_6, hidroxialquilo C_1 - C_6, hidroxialquenilo C_2 - C_6, -hidroxialquenilo C_2 - C_6, halo, -OH, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, - $S(O)_nR^{11}$ y -$S(O)_nNR^{11}R^{12}$;

R^{11} y R^{12} en cada caso se seleccionan independientemente cada uno entre H, alquilo C_1 - C_8, cicloalquilo C_3 - C_8, cicloalquenilo C_4 - C_8, bi- o

tricicloalquilo (C_5 - C_{11}), bi- o tricicloalquenilo (C_7 - C_{11}), heterocicloalquilo de (entre 3 y 8 miembros), arilo C_6 - C_{10} y heteroarilo de (entre 5 y 14 miembros), en el que dicho alquilo de R^{11} está opcional e independientemente sustituido con entre uno y tres sustituyentes seleccionados independientemente entre -OH, - CN y cicloalquilo C_3 - C_8, y en el que cada átomo de hidrógeno de dicho alquilo está opcional e independientemente reemplazado con un átomo halo, y en el que dicho cicloalquilo, cicloalquenilo, heterocicloalquilo, arilo y heteroarilo de R^{11} están cada uno de ellos opcional e independientemente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre halo, alquilo C_1 - C_8 opcionalmente sustituido con entre uno a tres átomos halo, -OH, -CN y cicloalquilo C_3 - C_8; y

n es en cada caso un número entero seleccionado independientemente entre cero, 1 y 2;

o una sal farmacéuticamente aceptable de los mismos.

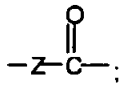
En un aspecto de la realización anterior, R^7 es un -cicloalquilo C_4 - C_8, -heterocicloalquilo de (entre 4 y 10 miembros), -arilo C_6 - C_{14}, o -heteroarilo de (entre 5 y 15 miembros), sustituido con un -alquilo C_1 - C_4 y en el que dicho alquilo está sustituido adicionalmente con R^{7C}, en el que R^{7C} es $-NR^9R^{10}$.

En otro aspecto de la realización anterior, R^9 es hidrógeno o metilo, R^{10} es -alquilo C_1 - C_8, o -cicloalquilo C_4 - C_8, en el que dicho alquilo o cicloalquilo de R^{10} está opcionalmente sustituido con entre uno a seis sustituyentes seleccionados entre R^{10a} en el que R^{10a} se selecciona entre halo, -alquilo C_1 – C_4, o -cicloalquilo C_4 - C_8, -heteroarilo de (entre 5 y 15 miembros), o -hidroxialquilo C_1 - C_4; o $-NR^9R^{10}$ es un heterocicloalquilo de (entre 4 y 6 miembros) opcionalmente sustituido con entre uno y seis sustituyentes

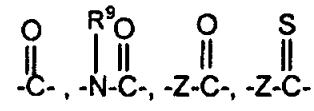
seleccionados entre halo, -alquilo C_1 - C_4 o -hidroxialquilo C_1 - C_4.

En otro aspecto de la realización anterior, R^7 es un -alquilo C_1 - C_8 sustituido con un -cicloalquilo C_4 - C_8; -bi- o tricicloalquilo (C_5 - C_{20}), heterocicloalquilo de (entre 4 y 8 miembros), -heterobi- o heterotricicloalquilo de (entre 7 y 12 miembros), -arilo C_6 - C_{14}, -benzo(cicloalquilo C_3 - C_8), -heteroarilo de entre (5 y 15 miembros), en el que R^7 está opcionalmente sustituido independientemente con entre uno y seis sustituyentes seleccionados independientemente entre R^{7a}, en el que R^{7a} es $-NR^9R^{10}$, halo, -alquilo C_1 - C_4 o -hidroxialquilo C_1 - C_4.

En otro aspecto de la realización anterior R^7 es un -alquilo C_1 - C_6 sustituido con heterocicloalquilo de (entre 4 y 8 miembros) o -arilo C_6 - C_{14}, en el que R^7 está opcionalmente sustituido con independientemente entre uno y seis sustituyentes seleccionados independientemente entre R^{7a}, en el que R^{7a} es $-NR^9R^{10}$, halo, -OH, -alquilo C_1 - C_4 o -hidroxialquilo C_1 - C_4, en el que dicho alquilo o hidroxialquilo está opcionalmente sustituido con entre uno y seis halo.

En otro aspecto de la realización anterior opcionalmente A está ausente y R^1 es -benzo (cicloalquilo C_5 - C_6) sustituido opcionalmente con entre uno a tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_6, halo y OH; o A es  ; Z es $-CH_2$, -CH(OH) o -CH(alquilo C_1 - C_6) y R^1 es alquilo C_1 - C_{10}, arilo C_6 - C_{10}, o heteroarilo de (entre 6 y 10 miembros), en el que dicho alquilo, arilo y heteroarilo están opcionalmente sustituidos con entre uno y tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_6, halo, y OH; R^2 es H o alquilo C_1 - C_6; R^3 es H, $-CH_2CH_2SCH_3$, $-CH_2CH_2OCH_3$, o alquilo C_1 - C_6; R^4 es H y R^6 es H o -alquilo C_1 - C_6.

En otra realización, la presente invención se refiere a compuestos de fórmula I en la que A está ausente o se selecciona entre



Z se selecciona entre $-CH_2$, -CH(OH), -CH(alquilo C_1 - C_6), -CH(alcoxi C_1 - C_6), $-CH(NR^9R^{10})$, $-CH(CH_2(OH))$, -CH(CH(alquilo C_1 - C_4)(OH)) y -CH(C(alquil C_1 - C_4) (alquilo C_1 - C_4)(OH));

R^1 se selecciona entre -alquilo C_1 - C_{20}, -alquenilo C_2 - C_{20}, alquinilo C_2 - C_{20}, -alcoxi C_1 - C_{20}, -alquenoxi C_2 - C_{20}, -hidroxialquilo C_1 - C_{20}, -cicloalquilo C_3 - C_8, benzo(cicloalquilo C_3 - C_8), benzo(heterocicloalquilo C_3 - C_8), -cicloalquenilo C_4 - C_8, -bi- o tricicloalquilo (C_5 - C_{11}), benzo bi o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 3 a 8 miembros), -arilo C_6 - C_{14} y -heteroarilo (de 5 a 14 miembros), en el que R^1 está opcionalmente sustituido con R^{1a};

en el que R^{1a} se selecciona independientemente entre -OH, halo, -alcoxi C_1 - C_6, -CN, $-NO_2$, $-NR^9R^{10}$, -C- $(=O)NR^9R^{10}$, $-C(=O)R^{11}$, $-C(=O)OR^{12}$, $-SO_2-NR^9R^{10}$, $-S(O)_n-R^{11}$, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

en la que dicho alcoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{1a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{1b};

en la que R^{1b} se selecciona en cada caso independientemente entre -

OH, - alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, - alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -NR^9R^{10}, -C-(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

R^2 se selecciona entre H, -alquilo C_1 - C_6, -alquenilo C_2 - C_6, -cicloalquilo C_3 - C_8 y -cicloalquenilo C_3 - C_8, en el que R^2 está sustituido opcional e independientemente con entre uno a tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, alcoxi C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, halo y –OH;

o R^1 y R^2 junto con el grupo A cuando está presente y el átomo de nitrógeno al que R^2 está unido, o R^1 y R^2 junto con el átomo de nitrógeno al que R^1 y R^2 están unidos cuando A está ausente, pueden opcionalmente formar un anillo de cuatro a ocho miembros;

R^3 se selecciona entre H, -alquilo C_1 - C_6, -alquenilo C_2 - C_6, -alquinilo C_2 - C_6, -cicloalquilo C_3 - C_6, -cicloalquenilo C_5 - C_6 y heterocicloalquilo de (entre 3 y 8 miembros), -arilo C_6 - C_{14} y heteroarilo de (entre 5 y 14 miembros), en el que dicho alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquenilo, heterocicloalquilo, arilo o heteroarilo están cada uno de ellos opcional e independientemente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre -alcoxi C_1 - C_4, halo, -OH, -S alquilo (C_1 - C_4), -alquilo (C_1 - C_4), -C(=O)OR^9, -SO_2R^9 y heterocicloalquilo de (entre 3

y 8 miembros) en el que dicho alquilo, alcoxi, y heterocicloalquilo puede estar adicionalmente sustituido con uno a seis halo;

R^4 es H, alquilo C_1 - C_6 o halo;

o R^3 y R^4 pueden junto con el átomo de carbono al que están unidos opcionalmente formar un resto seleccionado entre ciclopropilo, ciclobutilo, ciclopentilo, ciclohexilo, morfolino, piperidino, pirrolidino, tetrahidrofuranilo y perhidro-2H-pirano, en el que dicho resto formado por R^3 y R^4 está opcionalmente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, alcoxi C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, halo, -OH, -CN y alilo;

R^6 se selecciona entre H, -alquilo C_1 - C_6, -alquileno C_2 - C_6, -alcoxi C_1 - C_6, halo, -CN, cicloalquilo C_3 - C_{12}, cicloalquenilo C_4 - C_{12}, heteroarilo de (entre 5 y 10 miembros) y -arilo C_6 - C_{10}, en el que dicho alquilo, alquileno y alcoxi de R^6 están cada uno de ellos opcional e independientemente sustituidos con entre uno a tres sustituyentes seleccionados independientemente entre halo y -CN, y en el que dicho cicloalquilo, cicloalquenilo, heteroarilo y arilo de R^6 están cada uno de ellos opcional e independientemente sustituidos con entre uno a tres sustituyentes seleccionados independientemente entre -alquilo C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, halo y -CN;

R^7 se selecciona entre -alquilo C_1 - C_{20}, -alcoxi C_1 - C_{20}, -hidroxialquilo C_1 - C_{20}, -cicloalquilo C_3 - C_{12}, -cicloalquenilo C_4 - C_{12}, -bi- o tricicloalquilo (C_5 - C_{20}), -bi- o tricicloalquenilo (C_7 - C_{20}), heterocicloalquilo de (entre 3 y 12 miembros), -heterobi- o heterotricicloalquilo de (entre 7 y 20 miembros), -arilo C_6 - C_{14},

heteroarilo de (entre 5 y 15 miembros), -ariloxi C_6 - C_{15} y -heteroariloxi de (entre 5 y 15 miembros), en el que dichos alquilo, alquenilo, alquinilo, alcoxi, alquenoxi, alquinoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^7 están cada uno de ellos independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo de R^{7a} o están cada uno de ellos opcional e independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo de R^{7d};

en la que R^{7a} en cada caso se selecciona independientemente entre - alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, $-NR^9R^{10}$, $-C(=O)NR^9R^{10}$, -cicloalquilo C_3 - C_{15}, -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alquilo, alcoxi, alcoxialquilo, cicloalquilo, heterocicloalquilo, arilo, heteroarilo, ariloxi, y heteroariloxi de R^{7a} están cada uno independientemente sustituidos con R^{7b};

en la que R^{7d} en cada caso se selecciona independientemente entre - alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, $-NR^9R^{10}$, $-C(=O)NR^9R^{10}$, $-SO_2-NR^9R^{10}$, -cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), en el que dicho alquenilo, alquinilo, hidroxialquilo, alquenoxi, alquinoxi, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, de R^{7d} están cada uno de ellos opcionalmente sustituidos independientemente con entre uno y seis independientemente sustituyentes seleccionados entre el grupo R^{7b};

en la que R^{7b} en cada caso se selecciona independientemente entre - alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -

hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2- NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

o R^6 y R^7 pueden junto con los átomos de carbono y nitrógeno a los que están respectivamente unidos opcionalmente formar un anillo heterocicloalquilo de (entre 5 y 8 miembros), un anillo heterocicloalquenilo de (entre 5 y 8 miembros) o un anillo heteroarilo de (entre 6 y 8 miembros) , en el que dichos anillos heterocicloalquilo, heterocicloalquenilo y heteroarilo están opcional e independientemente sustituidos cada uno con entre uno a tres sustituyentes seleccionados independientemente entre halo, -alquilo C_1 - C_6, opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, -hidroxialquilo C_1 - C_6, -OH, -$(CH_2)_{cero\text{ - }10}$ NR^9R^{10}, -$(CH_2)_{cero\text{ - }10}$ $C(=O)NR^9R^{10}$, -$SO_2NR^9R^{10}$ y -cicloalquilo C_3 - C_{12};

R^9 y R^{10} se seleccionan en cada caso cada uno de ellos independientemente entre H, -$C(=O)R^{13}$ o -alquilo C_1 - C_{20}, en el que al menos uno de R^9 y R^{10} son -$C(=O)R^{13}$ o -alquilo C_1 - C_{20}, y en el que cada -alquilo C_1 - C_{20}, está sustituido con R^{10a};

en la que R^{10a} en cada caso se selecciona independientemente entre -alcoxi C_1 - C_6, -CN, -NO_2, -$NR^{11}R^{11}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, -cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de

4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alcoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{10a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{10b};

en la que R^{10b} en cada caso se selecciona independientemente entre -OH, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, $-NO_2$, $-NR^{11}R^{12}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-SO_2-NR^{11}R^{12}$, $-S(O)_n-R^{11}$, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

o NR^9R^{10} puede formar un heterocicloalquilo de (entre 4 y 20 miembros), heterobi- o tricicloalquilo de (entre 5 y 18 miembros), heterobi- o tricicloalquenilo de (entre 5 y 18 miembros), o heteroarilo de (entre 5 y 15 miembros), en el que dicho heterocicloalquilo, heterobi- o tricicloalquilo, heterobi- o tricicloalquenilo o heteroarilo están opcionalmente e independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre alquilo C_1 - C_6, -alquenilo C_2 - C_6, -alquenilo C_2 - C_6, alcoxi C_1 - C_6, alquenoxi C_2 - C_6, alquinoxi C_2 - C_6, hidroxialquilo C_1 - C_6, hidroxialquenilo C_2 - C_6, -hidroxialquenilo C_2 - C_6, halo, -OH, -CN, $-NO_2$, $-NR^{11}R^{12}$, $-C(=O)NR^{11}R^{12}$ $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-S(O)_nR^{11}$ y $-S(O)_nNR^{11}R^{12}$;

R^{11} y R^{12} en cada caso se seleccionan independientemente cada uno entre H, alquilo C_1 - C_8, cicloalquilo C_3 - C_8, cicloalquenilo C_4 - C_8, bi- o tricicloalquilo (C_5 - C_{11}), bi- o tricicloalquenilo (C_7 - C_{11}), heterocicloalquilo de (entre 3 y 8 miembros), arilo C_6 - C_{10} y heteroarilo de (entre 5 y 14 miembros), en el que dicho alquilo de R^{11} y R^{12} está opcional e independientemente sustituido con entre uno y tres sustituyentes seleccionados independientemente entre -OH, - CN y cicloalquilo C_3 - C_8, y en el que cada átomo de hidrógeno de dicho alquilo está opcional e independientemente reemplazado con un átomo halo, y en el que dicho cicloalquilo, cicloalquenilo, heterocicloalquilo, arilo y heteroarilo de R^{11} y R^{12} están cada uno de ellos opcional e independientemente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre halo, alquilo C_1 - C_8 opcionalmente sustituido con entre uno a tres átomos halo, -OH, -CN y -cicloalquilo C_3 - C_8;

R^{13} en cada caso se selecciona independientemente entre alquilo sustituido con -alcoxi C_1 - C_{12}, cicloalquilo C_3 – C_{15}, cicloalquenilo C_4 - C_{15}, bi- o tricicloalquilo (C_5 - C_{11}), -bi- o -tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo de (entre 4 y 20 miembros), arilo C_6 - C_{15}, heteroarilo de (entre 5 y 15 miembros), -ariloxi C_6 - C_{15} y -heteroariloxi de (entre 5 y 15 miembros); en el que dicho alcoxi, cicloalquilo, cicloalquenilo, -bi- o -tricicloalquilo, -bi- o -tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{13} está opcionalmente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre halo, -alquilo C_1 - C_8 opcionalmente sustituido con entre uno a tres átomos halo, -OH, -CN y -cicloalquilo C_3 - C_8; y

n es en cada caso un número entero seleccionado independientemente entre cero, 1 y 2;

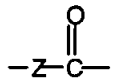
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o una sal farmacéuticamente aceptable de los mismos.

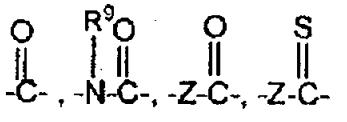
En un aspecto de la realización anterior, R^7 es un -alquilo C_1 - C_8 sustituido con R^{7a}; R^{7a} es $-NR^9R^{10}$; R^9 es H o metilo; R^{10} es un -alquilo C_1 - C_8; R^{10a} es -alcoxi C_1 - C_6, -cicloalquilo C_4 - C_8, -heterocicloalquilo de (entre 4 y 8 miembros), arilo C_6 - C_{15} o heteroarilo de (entre 5 y 15 miembros), en el que dicho alcoxi, cicloalquilo, heterocicloalquilo, arilo, heteroarilo de R^{10a} están cada uno de ellos opcional e independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo de R^{10b}; en el que R^{10b} es halo, -OH, -alquilo C_1 - C_4 o -hidroxialquilo C_1 - C_4, en el que dicho alquilo o hidroxialquilo de R^{10b} está opcionalmente sustituido con uno a seis halo.

En otro aspecto de la realización anterior, R^7 es un -alquilo C_1 - C_8 sustituido con R^{7a}; R^{7a} es $-C(=O)NR^9R^{10}$; R^9 es H o metilo; R^{10} es un alquilo C_1 - C_8; R^{10a} es alcoxi C_1 - C_6, -cicloalquilo C_4 - C_8, -heterocicloalquilo de (entre 4 y 8 miembros), arilo C_6 - C_{15} o heteroarilo de (entre 5 y 15 miembros), en el que dicho alcoxi, cicloalquilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{10a} están cada uno de ellos opcional e independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo de R^{10b}; en el que R^{10b} es halo, -OH, -alquilo C_1 - C_4 o -hidroxialquilo C_1 - C_4, en el que dicho alquilo o hidroxialquilo de R^{10b} está opcionalmente sustituido con uno a seis halo.

En otro aspecto de la realización anterior, A está ausente y R^1 es -benzo (cicloalquilo C_5 - C_6) opcionalmente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_6, halo y OH; o A es

 : Z es $-CH_2$, -CH(OH) o -CH(alquilo C_1 - C_6) y R^1 es alquilo C_1 - C_{10}, arilo C_6 - C_{10}, o heteroarilo de (entre 6 y 10 miembros), en el que dicho alquilo, arilo y heteroarilo están opcionalmente sustituidos independientemente con entre uno y tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_6, halo, y OH; R^2 es H o alquilo C_1 - C_6; R^3 es H, $-CH_2CH_2SCH_3$, $-CH_2CH_2OCH_3$, o alquilo C_1 - C_6; R^4 es H y R^6 es H o alquilo C_1 - C_6.

En otra realización, la presente invención se refiere a compuestos de fórmula I en la que A está ausente o se selecciona entre



Z se selecciona entre $-CH_2$, -CH(OH), -CH(alquilo C_1 - C_6), -CH(alcoxi C_1 - C_6), $-CH(NR^9R^{10})$, $-CH(CH_2(OH))$, -CH(CH(alquilo C_1 - C_4)(OH)) y -CH(C(alquil C_1 - C_4) (alquilo C_1 - C_4)(OH));

R^1 se selecciona entre -alquilo C_1 - C_{20}, -alquenilo C_2 - C_{20}, alquinilo C_2 - C_{20}, -alcoxi C_1 - C_{20}, -alquenoxi C_2 - C_{20}, -hidroxialquilo C_1 - C_{20}, -cicloalquilo C_3 - C_8, benzo(cicloalquilo C_3 - C_8), benzo(heterocicloalquilo C_3 - C_8), -cicloalquenilo C_4 - C_8, -bi- o tricicloalquilo (C_5 - C_{11}), benzo bi o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 3 a 8 miembros), -arilo C_6 - C_{14} y -heteroarilo (de 5 a 14 miembros), en el que R^1 está opcionalmente sustituido con R^{1a};

en el que R^{1a} se selecciona independientemente entre -OH, halo, -alcoxi C_1 - C_6, -CN, $-NO_2$, $-NR^9R^{10}$, -C- (=O)NR^9R^{10}, $-C(=O)R^{11}$, $-C(=O)OR^{12}$, $-SO_2-NR^9R^{10}$, $-S(O)_n-R^{11}$, -cicloalquilo C_3 - C_{15}, -cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de

4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

en la que dicho alcoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{1a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{1b};

en la que R^{1b} se selecciona en cada caso independientemente entre -OH, - alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, $-NO_2$, $-NR^9R^{10}$, $-C(=O)NR^9R^{10}$, $-C(=O)R^{11}$, $-C(=O)OR^{12}$, $-SO_2-NR^9R^{10}$, $-S(O)_n-R^{11}$, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

R^2 se selecciona entre H, -alquilo C_1 - C_6, -alquenilo C_2 - C_6, -cicloalquilo C_3 - C_8 y -cicloalquenilo C_3 - C_8, en el que R^2 está sustituido opcional e independientemente con entre uno a tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, alcoxi C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, halo y –OH;

o R^1 y R^2 junto con el grupo A cuando está presente y el átomo de nitrógeno al que R^2 está unido, o R^1 y R^2 junto con el átomo de nitrógeno al que R^1 y R^2 están unidos cuando A está ausente, pueden opcionalmente formar un anillo de cuatro a ocho miembros;

R^3 se selecciona entre -arilo C_6 - C_{14}, y heteroarilo de (entre 5 y 14

miembros), en el que dicho arilo o heteroarilo están cada uno de ellos opcional e independientemente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre -alcoxi C_1 - C_4, halo, -OH, -S alquilo (C_1 - C_4), -alquilo (C_1 - C_4), -C(=O)OR^9, -SO_2R^9 y heterocicloalquilo de (entre 3 y 8 miembros) en el que dicho alquilo, alcoxi, y heterocicloalquilo puede estar adicionalmente sustituido con uno a seis halo;

R^4 es H, alquilo C_1 - C_6 o halo;

o R^3 y R^4 pueden junto con el átomo de carbono al que están unidos opcionalmente formar un resto seleccionado entre ciclopropilo, ciclobutilo, ciclopentilo, ciclohexilo, morfolino, piperidino, pirrolidino, tetrahidrofuranilo y perhidro-2H-pirano, en el que dicho resto formado por R^3 y R^4 está opcionalmente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre -alquilo C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, halo, -OH, -CN y alilo;

R^6 se selecciona entre H, -alquilo C_1 - C_6, -alquileno C_2 - C_6, -alcoxi C_1 - C_6, halo, -CN, cicloalquilo C_3 - C_{12}, cicloalquenilo C_4 - C_{12}, heteroarilo de (entre 5 y 10 miembros) y -arilo C_6 - C_{10}, en el que dicho alquilo, alquileno y alcoxi de R^6 están cada uno de ellos opcional e independientemente sustituidos con entre uno a tres sustituyentes seleccionados independientemente entre halo y -CN, y en el que dicho cicloalquilo, cicloalquenilo, heteroarilo y arilo de R^6 están cada uno de ellos opcional e independientemente sustituidos con entre uno a tres sustituyentes seleccionados independientemente entre -alquilo C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, halo y -CN;

R^7 se selecciona entre H, -alquilo C_1 - C_{20}, -alcoxi C_1 - C_{20}, -hidroxialquilo C_1 - C_{20}, -cicloalquilo C_3 - C_{12}, cicloalquenilo C_4 - C_{12}, -bi- o tricicloalquilo (C_5 - C_{20}), -bi- o tricicloalquenilo (C_7 - C_{20}), heterocicloalquilo de (entre 3 y 12 miembros), -heterobi- o heterotricicloalquilo de (entre 7 y 20 miembros), arilo C_6 - C_{14}, y heteroarilo de (entre 5 y 15 miembros), en el que dichos alquilo, alquenilo, alquinilo, alcoxi, alquenoxi, alquinoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^7 están cada uno de ellos opcional e independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo de R^{7a};

en la que R^{7a} en cada caso se selecciona independientemente entre -OH, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, - alcoxi C_1 - C_6, - alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alquilo, alquenilo, alquinilo, alcoxi, alquenoxi, alquinoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi, y heteroariloxi de R^{7a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo de R^{7b};

en la que R^{7b} en cada caso se selecciona independientemente entre -OH, -alquilo C_1 - C_{12}, alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -

alcoxialquilo C_1 - C_{12}, - hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, - NR^9R^{10}, -$C(=O)NR^9R^{10}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -SO_2- NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

o R^6 y R^7 pueden junto con los átomos de carbono y nitrógeno a los que están respectivamente unidos opcionalmente formar un anillo heterocicloalquilo de (entre 5 y 8 miembros), un anillo heterocicloalquenilo de (entre 5 y 8 miembros) o un anillo heteroarilo de (entre 6 y 8 miembros) , en el que dichos anillos heterocicloalquilo, heterocicloalquenilo y heteroarilo están opcional e independientemente sustituidos cada uno con entre uno a tres sustituyentes seleccionados independientemente entre halo, -alquilo C_1 - C_6, opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, -hidroxialquilo C_1 - C_6, -OH, -$(CH_2)_{cero\text{ - }10}$ NR^9R^{10}, -$(CH_2)_{cero\text{ - }10}$ $C(=O)NR^9R^{10}$, -$SO_2NR^9R^{10}$ y -cicloalquilo C_3 - C_{12};

R^9 y R^{10} en cada caso se seleccionan cada uno de ellos independientemente entre H, -OH, alquilo C_1 - C_{12}, alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, - hidroxialquilo C_1 - C_{12}, - alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, - SO_2- $NR^{10}R^{11}$, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), -ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros), en el que dicho alquilo, alquenilo,

alquinilo, alcoxi, alquenoxi, alquinoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^9 y R^{10} están cada uno de ellos opcionalmente sustituidos independientemente con entre uno y seis sustituyentes seleccionados independientemente entre el grupo de R^{10a};

en la que R^{10a} en cada caso se selecciona independientemente entre -OH, halo, - alcoxi C_1 - C_6, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, -cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alcoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{10a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{10b};

en la que R^{10b} en cada caso se selecciona independientemente entre -OH, halo, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, -cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), -ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

o NR^9R^{10} puede formar un heterocicloalquilo de (entre 4 y 20 miembros), heterobi- o tricicloalquilo de (entre 5 y 18 miembros), heterobi- o

tricicloalquenilo de (entre 5 y 18 miembros), o heteroarilo de (entre 5 y 15 miembros), en el que dicho heterocicloalquilo, heterobi- o tricicloalquilo, heterobi- o tricicloalquenilo o heteroarilo están opcionalmente e independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre -alquilo C_1 - C_6, -alquenilo C_2 - C_6, - alquenilo C_2 - C_6, - alcoxi C_1 - C_6, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, - hidroxialquilo C_1 - C_6, - hidroxialquenilo C_2 - C_6, - hidroxialquenilo C_2 - C_6, halo, -OH, -CN, $-NO_2$, $-NR^{11}R^{12}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-S(O)_nR^{11}$ y $-S(O)_nNR^{11}R^{12}$;

en el que R^{11} y R^{12} en cada caso se seleccionan independientemente cada uno entre H, -alquilo C_1 - C_8, -cicloalquilo C_3 - C_8, -cicloalquenilo C_4 - C_8, bi- o tricicloalquilo (C_5 - C_{11}), bi- o tricicloalquenilo (C_7 - C_{11}), heterocicloalquilo de (entre 3 y 8 miembros), -arilo C_6 - C_{10} y -heteroarilo de (entre 5 y 14 miembros), en el que dicho alquilo de R^{11} está opcional e independientemente sustituido con entre uno y tres sustituyentes seleccionados independientemente entre - OH, - CN y cicloalquilo C_3 - C_8, y en el que cada átomo de hidrógeno de dicho alquilo está opcional e independientemente reemplazado con un átomo halo, y en el que dicho cicloalquilo, cicloalquenilo, heterocicloalquilo, arilo y heteroarilo de R^{11} están cada uno de ellos opcional e independientemente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre halo, alquilo C_1 - C_8 opcionalmente sustituido con entre uno a tres átomos halo, -OH, -CN y cicloalquilo C_3 - C_8; y

n es en cada caso un número entero seleccionado independientemente entre cero, 1 y 2;

o una sal farmacéuticamente aceptable de los mismos.

En otra realización, la presente invención se refiere a compuestos de fórmula I, en la que A está ausente;

R^1 es -alquilo C_1 - C_{20}; en el que R^1 está sustituido independientemente con entre uno y seis sustituyentes seleccionados independientemente entre R^{1a};

en la que R^{1a} en cada caso se selecciona independientemente entre -alcoxi C_1 - C_6, -CN, -cicloalquilo C_3 - C_{15}, -cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

en la que dicho cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{1a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{1b};

en la que R^{1b} se selecciona en cada caso independientemente entre -OH, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, $-NO_2$, $-NR^9R^{10}$, $-C-(=O)NR^9R^{10}$, $-C(=O)R^{11}$, $-C(=O)OR^{12}$, $-SO_2-NR^9R^{10}$, $-S(O)_n-R^{11}$, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

R^2 se selecciona entre H, -alquilo C_1 - C_6, -alquenilo C_2 - C_6, -cicloalquilo C_3 - C_8 y cicloalquenilo C_3 - C_8, en el que R^2 está sustituido opcional e independientemente con entre uno a tres sustituyentes seleccionados

independientemente entre alquilo C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, halo y -OH.

R^3 se selecciona entre H, -alquilo C_1 - C_6, -alquenilo C_2 - C_6, -alquinilo C_2 - C_6, -cicloalquilo C_3 - C_6, -cicloalquenilo C_5 - C_6 y heterocicloalquilo de (entre 3 y 8 miembros), -arilo C_6 - C_{14} y heteroarilo de (entre 5 y 14 miembros), en el que dicho alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquenilo, heterocicloalquilo, arilo o heteroarilo están cada uno de ellos opcional e independientemente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre alcoxi C_1 - C_4, halo, -OH, -S alquilo (C_1 - C_4), -alquilo (C_1 - C_4), $-C(=O)OR^9$, $-SO_2R^9$ y heterocicloalquilo de (entre 3 y 8 miembros) en el que dicho alquilo, alcoxi, y heterocicloalquilo puede estar adicionalmente sustituido con uno a seis halo;

R^4 es H, alquilo C_1 - C_6 o halo;

o R^3 y R^4 pueden junto con el átomo de carbono al que están unidos opcionalmente formar un resto seleccionado entre ciclopropilo, ciclobutilo, ciclopentilo, ciclohexilo, morfolino, piperidino, pirrolidino, tetrahidrofuranilo y perhidro-2H-pirano, en el que dicho resto formado por R^3 y R^4 está opcionalmente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre -alquilo C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, halo, -OH, -CN y alilo;

R^6 se selecciona entre H, -alquilo C_1 - C_6, -alquileno C_2 - C_6, -alcoxi C_1 - C_6, halo, -CN, -cicloalquilo C_3 - C_{12}, -cicloalquenilo C_4 - C_{12}, heteroarilo de (entre 5 y 10 miembros) y -arilo C_6 - C_{10}, en el que dicho alquilo, alquileno y alcoxi de

R^6 están cada uno de ellos opcional e independientemente sustituidos con entre uno a tres sustituyentes seleccionados independientemente entre halo y -CN, y en el que dicho cicloalquilo, cicloalquenilo, heteroarilo y arilo de R^6 están cada uno de ellos opcional e independientemente sustituidos con entre uno a tres sustituyentes seleccionados independientemente entre -alquilo C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, halo y -CN;

R^7 se selecciona entre H, -alquilo C_1 - C_{20}, -alcoxi C_1 - C_{20}, -hidroxialquilo C_1 - C_{20}, -cicloalquilo C_3 - C_{12}, -cicloalquenilo C_4 - C_{12}, bi- o tricicloalquilo (C_5 - C_{20}), bi- o tricicloalquenilo (C_7 - C_{20}), -heterocicloalquilo de (entre 3 y 12 miembros), -heterobi o o heterotricicloalquilo de (entre 7 y 20 miembros) , -arilo C_6 - C_{14}, y -heteroarilo de (entre 5 y 15 miembros) en el que dichos alquilo, alquenilo, alquinilo, alcoxi, alquenoxi, alquinoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^7están cada uno de ellos opcional e independientemente sustituido con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{7a};

en la que R^{7a} en cada caso se selecciona independientemente entre -OH, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alquilo, alquenilo,

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alquinilo, alcoxi, alquenoxi, alquinoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{7a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{7b};

en la que R^{7b} en cada caso se selecciona independientemente entre -OH, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, $-NO_2$, $-NR^9R^{10}$, $-C(=O)NR^9R^{10}$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-SO_2-NR^9R^{10}$, $-S(O)_n-R^{11}$, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

o R^6 y R^7 pueden junto con los átomos de carbono y nitrógeno a los que están respectivamente unidos opcionalmente formar un anillo heterocicloalquilo de (entre 5 y 8 miembros), un anillo heterocicloalquenilo de (entre 5 y 8 miembros) o un anillo heteroarilo de (entre 6 y 8 miembros) , en el que dichos anillos heterocicloalquilo, heterocicloalquenilo y heteroarilo están opcional e independientemente sustituidos cada uno con entre uno a tres sustituyentes seleccionados independientemente entre halo, -alquilo C_1 - C_6, opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, -hidroxialquilo C_1 - C_6, -OH, $-(CH_2)_{cero\text{ - }10}NR^9R^{10}$, $-(CH_2)_{cero\text{ - }10}C(=O)NR^9R^{10}$, $-SO_2NR^9R^{10}$ y cicloalquilo C_3 - C_{12};

R^9 y R^{10} en cada caso se seleccionan cada uno de ellos

independientemente entre H, -OH, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6 -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, - alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, $-C(=O)NR^{11}R^{12}$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-SO_2-NR^{11}R^{12}$, $-S(O)_n-R^{11}$, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alquilo, alquenilo, alquinilo, alcoxi, alquenoxi, alquinoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^9 y R^{10} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{10a};

en la que R^{10a} en cada caso se selecciona independientemente entre -OH, halo, -alcoxi C_1 - C_6, -CN, $-NO_2$, $-NR^{11}R^{12}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)R^{11}$, $-C(=O)OR^{12}$, $-SO_2-NR^{11}R^{12}$, $-S(O)_n-R^{11}$, -cicloalquilo C_3 - C_{15}, -cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), - heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alcoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{10a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{10b};

en la que R^{10b} en cada caso se selecciona independientemente entre -OH, halo, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 -

C_6, halo, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

o NR^9R^{10} puede formar un heterocicloalquilo de (entre 4 y 20 miembros), heterobi- o tricicloalquilo de (entre 5 y 18 miembros), heterobi- o tricicloalquenilo de (entre 5 y 18 miembros), o heteroarilo de (entre 5 y 15 miembros), en el que dicho heterocicloalquilo, heterobi- o tricicloalquilo, heterobi- o tricicloalquenilo o heteroarilo están opcionalmente e independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre -alquilo C_1 - C_6, -alquenilo C_2 - C_6, -alquenilo C_2 - C_6, - alcoxi C_1 - C_6, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, -hidroxialquilo C_1 - C_6, - hidroxialquenilo C_2 - C_6, - hidroxialquenilo C_2 - C_6, halo, -OH, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, - $C(=O)R^{11}$, -$C(=O)OR^{11}$, - $S(O)_nR^{11}$ y -$S(O)_nNR^{11}R^{12}$;

R^{11} y R^{12} en cada caso se seleccionan independientemente cada uno entre H, alquilo C_1 - C_8, cicloalquilo C_3 - C_8, cicloalquenilo C_4 - C_8, bi- o tricicloalquilo (C_5 - C_{11}), bi- o tricicloalquenilo (C_7 - C_{11}), heterocicloalquilo de (entre 3 y 8 miembros), arilo C_6 - C_{10} y heteroarilo de (entre 5 y 14 miembros), en el que dicho alquilo de R^{11} está opcional e independientemente sustituido con entre uno y tres sustituyentes seleccionados independientemente entre -OH, - CN y cicloalquilo C_3 - C_8, y en el que cada átomo de hidrógeno de dicho alquilo está opcional e independientemente reemplazado con un átomo halo, y en el que dicho cicloalquilo, cicloalquenilo, heterocicloalquilo, arilo y heteroarilo

de R^{11} están cada uno de ellos opcional e independientemente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre halo, alquilo C_1 - C_8 opcionalmente sustituido con entre uno a tres átomos halo, -OH, -CN y cicloalquilo C_3 - C_8; y

n es en cada caso un número entero seleccionado independientemente entre cero, 1 y 2;

o una sal farmacéuticamente aceptable de los mismos.

Los compuestos de la fórmula I pueden tener centros ópticos y por lo tanto pueden aparecer en diferentes configuraciones enantioméricas y diastereoméricas. La presente invención incluye todos los enantiómeros, diastereómeros, y otros estereoisómeros de tales compuestos de la fórmula I, así como compuestos racémicos y las mezclas racémicas y otras mezclas de estereoisómeros de los mismos.

Las sales farmacéuticamente aceptables de los compuestos de fórmula I incluyen las sales de adición de ácidos y básicas de los mismos.

Las sales de adición de ácidos adecuadas se forman a partir de ácidos que forman sales no tóxicas. Los ejemplos incluyen, pero no se limitan a, las sales acetato, adipato, aspartato, benzoato, besilato, bicarbonato/carbonato, bisulfato/sulfato, borato, camsilato, citrato, ciclamato, edisilato, esilato, formiato, fumarato, gluceptato, gluconato, glucuronato, hexafluorofosfato, hibenzato, clorhidrato/cloruro, bromhidrato/bromuro, yodhidrato/yoduro, isetionato, lactato, malato, maleato, malonato, mandelatos, mesilato, metilsulfato, naftilato, 2-napsilato, nicotinato, nitrato, orotato, oxalato, palmitato, pamoato, fosfato/fosfato ácido/fosfato diácido, piroglutamato, salicilato, sacarato, estearato, succinato, sulfonato, estannato, tartrato, tosilato, trifluoroacetato y

xinofoato.

Las sales de base adecuadas se forman a partir de bases que forman sales no tóxicas. Los ejemplos incluyen, pero no se limitan a, las sales de aluminio, de arginina, de benzatina, de calcio, de colina, de dietilamina, de diolamina, de glicina, de lisina, de magnesio, de meglumina, de olamina, de potasio, de sodio, de trometamina y de cinc.

También se pueden formar hemisales de ácidos y bases, por ejemplo, hemisulfatos y sales de hemicalcio.

Para una revisión sobre las sales adecuadas, véase Handbook of Pharmaceutical Salts: Properties, Selection, and Use por Stahl y Wermuth (Wiley - VCH, 2002).

Las sales farmacéuticamente aceptables de los compuestos de fórmula I se pueden preparar mediante uno o más de tres procedimientos:

(i) hacer reaccionar el compuesto de fórmula I con el ácido o base deseado;

(ii) retirar un grupo protector lábil a ácido o base de un precursor adecuado del compuesto de fórmula I o mediante la apertura de anillo de un precursor cíclico adecuado, por ejemplo, una lactona o lactama, usando el ácido o base deseado; o

(iii) convertir una sal del compuesto de fórmula I en otra mediante reacción con un ácido o base apropiado o mediante una columna de intercambio iónico adecuada.

Típicamente las tres reacciones se llevan a cabo en solución. La sal resultante puede precipitar y recogerse por filtración o se puede recuperar mediante evaporación del disolvente. El grado de ionización en la sal resultante

puede variar entre completamente ionizada y casi no ionizada.

Los compuestos de la invención pueden existir en un continuo de estados sólidos que varía entre totalmente amorfo hasta totalmente cristalino. El término 'amorfo' se refiere a un estado en el que el material carece de ordenación de alto rango a nivel molecular y, dependiendo de la temperatura, puede mostrar las propiedades físicas de un sólido o un líquido. Típicamente tales materiales no proporcionan patrones de difracción de rayos X característicos y, aunque muestran las propiedades de un sólido, se describen más formalmente como un líquido. Tras calentamiento, se produce un cambio de las propiedades sólidas a líquidas que se caracteriza por un cambio de estado, típicamente de segundo orden ('transición al estado vítreo"). El término 'cristalino' se refiere a una fase sólida en la que el material tiene una estructura interna ordenada regular a nivel molecular y proporciona un patrón de difracción de rayos X característico con picos definidos. Tales materiales cuando se calientan suficientemente también mostrarán las propiedades de un líquido, pero el cambio de sólido a líquido se caracteriza por un cambio de fase, típicamente de primer orden ('punto de fusión').

Los compuestos de la invención también pueden existir en formas no solvatadas y solvatadas. El término 'solvato' se usa en esta memoria descriptiva para describir un complejo molecular que comprende el compuesto de la invención y una o más moléculas de disolvente farmacéuticamente aceptables, por ejemplo, etanol. El término 'hidrato' se emplea cuando dicho disolvente es agua.

Un sistema de clasificación actualmente aceptado para hidratos orgánicos es uno que define hidratos de sitio aislado, hidratos de canal, o

hidratos coordinados a iones metálicos - véase Polymorphism in Phamaceutical Solids por K. R. Morris (Ed. H. G. Brittain, Marcel Dekker, 1995). Los hidratos de sitio aislado son aquellos en los que las moléculas de agua están aisladas del contacto directo entre sí mediante moléculas orgánicas que intervienen. En los hidratos de canal, las moléculas de agua se encuentran en canales reticulares donde están cerca de otras moléculas de agua. En los hidratos coordinados a iones metálicos, las moléculas de agua están unidas al ion metálico.

Cuando el disolvente o agua está estrechamente unido, el complejo tendrá una estequiometría bien definida independiente de la humedad. Sin embargo, cuando el disolvente o agua está débilmente unido, como en solvatos de canal y compuestos higroscópicos, el contenido en agua/disolvente dependerá de la humedad y condiciones de secado. En tales casos, la no estequiometría será la norma.

Los compuestos de la invención también pueden existir en un estado mesomórfico (mesofase o cristal líquido) cuando se someten a condiciones adecuadas. El estado mesomórfico es intermedio entre el verdadero estado cristalino y el verdadero estado líquido (bien fundido o en solución). El mesomorfismo que surge como resultado de un cambio en la temperatura se describe como 'termotrópico' y el que resulta de la adición de un segundo componente, tal como agua u otro disolvente, se describe como 'liotrópico'. Los compuestos que tienen el potencial para formar mesofases liotrópicas se describen como 'anfifílicos' y constan de moléculas que poseen un grupo de cabeza iónico (tal como $-COO^-Na^+$, $-COO^-K^+$, o $-SO_3^-Na^+$) o no iónico (tal como $-N^-N^+(CH_3)_3$). Para más información, véase Crystals and the Polarizing

Microscope por N. H. Hartshorne y A. Stuart, edición 4ª (Edward Arnold, 1970).

De aquí en adelante todas las referencias a los compuestos de la fórmula I incluyen las referencias a sales, solvatos, complejos multicomponentes y cristales líquidos de los mismos y a solvatos, complejos multicomponentes y cristales líquidos de las sales de los mismos.

Los compuestos de la invención incluyen los compuestos de la fórmula I como se ha definido en esta memoria descriptiva anteriormente, incluyendo todos los polimorfismos y hábitos cristalinos de los mismos, profármacos e isómeros de los mismos (incluyendo los isómeros ópticos, geométricos y tautómeros) como se define en esta memoria descriptiva posteriormente y los compuestos marcados isotópicamente de la fórmula I.

Salvo que se indique otra cosa, como se usa en esta memoria descriptiva, el término "A está ausente" significa un enlace directo entre el nitrógeno y R^1 (es decir -N-R^1).

Salvo que se indique otra cosa, como se usa en esta memoria descriptiva, los términos "halógeno" y "halo" incluyen F, Cl, Br, y I.

Salvo que se indique otra cosa, como se usa en esta memoria descriptiva, el término "alquilo" incluye radicales hidrocarburos monovalentes saturados que tienen restos lineales o ramificados. Los ejemplos de grupos alquilo incluyen, pero no se limitan a, metilo, etilo, *n*-propilo, isopropilo, y *t*-butilo.

Salvo que se indique otra cosa, como se usa en esta memoria descriptiva, el término "alquenilo" incluye restos alquilo que tienen al menos un doble enlace carbono - carbono en el que alquilo es como se ha definido anteriormente. Los ejemplos de alquenilo incluyen, pero no se limitan a, etenilo

y propenilo.

Salvo que se indique otra cosa, como se usa en esta memoria descriptiva, el término "alquinilo" incluye restos alquilo que tienen al menos un triple enlace carbono - carbono en el que alquilo es como se ha definido anteriormente. Los ejemplos de grupos alquinilo incluyen, pero no se limitan a, etinilo y 2-propinilo.

Salvo que se indique otra cosa, como se usa en esta memoria descriptiva, el término "alcoxi", significa "alquil-O-", en el que "alquilo" es como se ha definido anteriormente. Los ejemplos de grupos "alcoxi" incluyen, pero no se limitan a, metoxi, etoxi, propoxi, butoxi, pentoxi y aliloxi.

Salvo que se indique otra cosa, como se usa en esta memoria descriptiva, el término "alquenoxi", significa "alquenil-O-", en el que "alquenilo" es como se ha definido anteriormente.

Salvo que se indique otra cosa, como se usa en esta memoria descriptiva, el término "cicloalquilo" incluye restos alquilo cíclicos saturados no aromáticos en el que alquilo es como se ha definido anteriormente. Los ejemplos de cicloalquilo incluyen, pero no se limitan a, ciclopropilo, ciclobutilo, ciclopentilo, ciclohexilo y cicloheptilo. Grupos "bicicloalquilo" y "tricicloalquilo" son grupos carbocíclicos saturados no aromáticos constituidos por dos o tres anillos respectivamente, en los que dichos anillos comparten al menos un átomo de carbono. Salvo que se indique otra cosa, para los propósitos de la presente invención, grupos bicicloalquilo incluyen grupos espiro y grupos de anillos condensados. Los ejemplos de grupos bicicloalquilo incluyen, pero no se limitan a, biciclo[3.1.0]hexilo, biciclo-[2.2.1]hep-1-ilo, norbornilo, espiro[4.5]decilo, espiro[4.4]nonilo, espiro[4.3]octilo, y espiro[4.2]heptilo. Un

ejemplo de un grupo tricicloalquilo es adamantanilo. Otros grupos cicloalquilo, bicicloalquilo, y tricicloalquilo se conocen en la técnica, y tales grupos están abarcados por las definiciones de "cicloalquilo", "bicicloalquilo" y "tricicloalquilo" en esta memoria descriptiva.

"Cicloalquenilo", "bicicloalquenilo", y "tricicloalquenilo" se refieren a restos no aromáticos carbocíclicos cicloalquilo, bicicloalquilo, y tricicloalquilo como se han definido anteriormente, excepto que comprenden uno o mas dobles enlaces carbono - carbono que conectan miembros de los anillos de carbono (un enlace doble "endocíclico") y/o uno o más dobles enlaces carbono - carbono que conectan un miembro de anillo de carbono y un carbono adyacente que no es de anillo (un enlace doble "exocíclico"). Los ejemplos de grupos cicloalquenilo incluyen, pero no se limitan a, ciclopentenilo, ciclobutenilo, y ciclohexenilo, y un ejemplo no limitante de un grupo bicicloalquenilo es norbornenilo. Otros grupos cicloalquenilo, bicicloalquenilo, y tricicloalquenilo se conocen en la técnica, y tales grupos se incluyen dentro de las definiciones de "cicloalquenilo", "bicicloalquenilo" y "tricicloalquenilo" en esta memoria descriptiva.

Los grupos cicloalquilo, cicloalquenilo, bicicloalquilo, y bicicloalquenilo también incluyen grupos que están sustituidos con uno o más restos oxo. Los ejemplos de tales grupos con restos oxo son oxociclopentilo, oxociclobutilo, oxociclopentenilo, y norcanforilo.

Como se usa en esta memoria descriptiva, el término "benzocicloalquilo" incluye, sin limitación, restos tales como tetrahidronaftilo, indanilo, 1,2-benzocicloheptanilo y similares.

Salvo que se indique otra cosa, como se usa en esta memoria

descriptiva, el término "arilo" incluye un radical orgánico derivado de un hidrocarburo aromático mediante la eliminación de un hidrógeno, tal como fenilo, naftilo, indenilo, indanilo, y fluorenilo. "Arilo" abarca grupos de anillos condensados en los que al menos un anillo es aromático.

Salvo que se indique otra cosa, como se usa en esta memoria descriptiva, los términos "heterocíclico" y "heterocicloalquilo" se refieren a grupos cíclicos no aromáticos que contienen uno o más heteroátomos, preferiblemente entre uno a cuatro heteroátomos, cada uno de ellos seleccionados entre O, S y N. Los grupos "heterobicicloalquilo" son grupos cíclicos de dos anillos no aromáticos, en los que dichos anillos comparten uno o dos átomos, y en los que al menos uno de los anillos contiene un heteroátomo (O, S, N). Los grupos heterobicicloalquilo para los propósitos de esta invención, y salvo que se indique otra cosa, incluyen grupos espiro y grupos de anillos condensados. Los grupos "heterotricicloalquilo" son grupos cíclicos de tres anillos no aromáticos, en los que dichos anillos están condensados entre sí o forman un grupo espiro (en otras palabras, al menos dos de dichos anillos comparten uno o dos átomos y el tercer anillo comparte uno o dos átomos con al menos uno de dichos dos anillos). Los grupos heterotricicloalquilo de los compuestos de la presente invención pueden incluir uno o más heteroátomos O, S y/o N. En una realización, cada anillo en el heterobicicloalquilo o heterotricicloalquilo contiene hasta cuatro heteroátomos (es decir, cero a cuatro heteroátomos, con tal que al menos un anillo contenga al menos un heteroátomo). Los grupos heterocicloalquilo, heterobicicloalquilo y heterotricicloalquilo de la presente invención pueden también incluir sistemas de anillos sustituidos con uno o más restos oxo. Los grupos heterocíclicos, que

incluyen los grupos heterobicíclicos y heterotricíclicos, pueden comprender enlaces dobles o triples, por ejemplo heterocicloalquenilo, heterobicicloalquenilo, y heterotricicloalquenilo. Los ejemplos de grupos heterocíclicos no aromáticos son aziridinilo, azetidinilo, pirrolidinilo, piperidinilo, azepinilo, piperazinilo, 1,2,3,6-tetrahidropiridinilo, oxiranilo, oxetanilo, tetrahidrofuranilo, tetrahidrotienilo, tetrahidropiranilo, tetrahidrotiopiranilo, morfolino, tiomorfolino, tioxanilo, pirrolinilo, indolinilo, 2H-piranilo, 4H-piranilo, dioxanilo, 1,3-dioxolanilo, pirazolinilo, dihidropiranilo, dihidrotienilo, dihidrofuranilo, pirazolidinilo, imidazolinilo, imidazolidinilo, 3-azabiciclo[3.1.0]hexanilo, 3-azabiciclo[4.1.0]heptanilo, quinolizinilo, quinuclidinilo, 1,4-dioxaespiro[4.5]decilo, 1,4-dioxaespiro[4.4]nonilo, 1,4-dioxaespiro[4.3]octilo, y 1,4-dioxaespiro[4.2]heptilo.

Salvo que se indique otra cosa, como se usa en esta memoria descriptiva "heteroarilo" se refiere a los grupos aromáticos que contienen uno o más heteroátomos (O, S, o N) preferiblemente entre uno a cuatro heteroátomos. Un grupo multicíclico que contiene uno o más heteroátomos en los que al menos un anillo del grupo es aromático es un grupo "heteroarilo". Los grupos heteroarilo de esta invención también pueden incluir sistemas de anillos sustituidos con uno o más restos oxo. Los ejemplos de grupos heteroarilo son piridinilo, piridazinilo, imidazolilo, pirimidinilo, pirazolilo, triazolilo, pirazinilo, quinolilo, isoquinolilo, 1,2,3,4-tetrahidroquinolilo, tetrazolilo, furilo, tienilo, isoxazolilo, tiazolilo, oxazolilo, isotiazolilo, pirrolilo, indolilo, bencimidazolilo, benzofuranilo, cinnolinilo, indazolilo, indolizinilo, ftalazinilo, triazinilo, 1,2,4-triazinilo, 1,3,5-triazinilo, isoindolilo, 1-oxoisoindolilo, purinilo, oxadiazolilo, tiadiazolilo, furazanilo, benzofurazanilo, benzotiofenilo, benzotriazolilo,

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benzotiazolilo, benzoxazolilo, quinazolinilo, quinoxalinilo, naftiridinilo, dihidroquinolilo, tetrahidroquinolilo, dihidroisoquinolilo, tetrahidroisoquinolilo, benzofurilo, furopiridinilo, pirrolopirimidinilo, y azaindolilo.

Salvo que de otra manera se indique lo contrario, todos los grupos anteriores derivados de hidrocarburos pueden estar opcionalmente sustituidos con uno o más átomos de halógeno (por ejemplo, $-CH_2F$, $-CHF_2$, $-CF_3$, -PhCl, etc.).

Salvo que se indique otra cosa, el término "uno o más sustituyentes" como se usa en esta memoria descriptiva se refiere a entre uno y el número máximo de sustituyentes posibles en base al número de sitios de unión disponibles.

Salvo que se indique de otra manera, todos los grupos anteriores derivados de hidrocarburos pueden tener hasta aproximadamente 1 a aproximadamente 20 átomos de carbono (por ejemplo, alquilo C_1 - C_{20}, alquenilo C_2 - C_{20}, cicloalquilo C_3 - C_{20}, heterocicloalquilo de 3 - 20 miembros; arilo C_6 - C_{20}, heteroarilo de 5 a 20 miembros, etc.) o 1 a aproximadamente 15 átomos de carbono (por ejemplo, alquilo C_1 - C_{15}, alquenilo C_2 - C_{15}, cicloalquilo C_3 - C_{15}, heterocicloalquilo de 3 a 15 miembros, arilo C_{63} - C_{15}, heteroarilo de 5 a 15 miembros, etc.), o 1 a aproximadamente 12 átomos de carbono, o 1 a aproximadamente 8 átomos de carbono, o 1 a aproximadamente 6 átomos de carbono.

Como aprecian los expertos en la técnica, el uso de la fórmula I es una conveniencia, y la invención se entiende que vislumbra y abarca cada una y todas las especies de más adelante como no obstante se identifican individualmente y se exponen en esta memoria descriptiva. Así pues, la

presente invención contempla cada especie separadamente y cualquiera y todas las combinaciones y permutaciones de especies que caen dentro de la fórmula I.

Los grupos anteriores, por derivarse de los compuestos enumerados anteriormente, pueden estar unidos por C o unidos por N cuando esto sea posible. Por ejemplo, un grupo derivado de pirrol puede ser pirrol-1-ilo (unido por N) o pirrol-3-ilo (unido por C). Los términos que se refieren a los grupos también abarcan todos los tautómeros posibles.

Como se ha indicado, los llamados 'profármacos' de los compuestos de fórmula I también están dentro del ámbito de la invención. Así pues ciertos derivados de los compuestos de fórmula I que pueden tener poca o ninguna actividad farmacológica por ellos mismos pueden, cuando se administran en el interior o sobre el cuerpo, convertirse en compuestos de fórmula I que tienen la actividad deseada, por ejemplo, mediante escisión hidrolítica. Tales derivados se denominan 'profármacos'. Información adicional sobre el uso de profármacos se puede encontrar en Pro - drugs as Novel Delivery Systems, vol. 14, ACS Symposium Series (T. Higuchi y W. Stella) y Bioreversible Carriers in Drug Design, Pergamon Press, 1987 (Ed. E. B. Roche, American Pharmaceutical Association).

Los profármacos de acuerdo con la invención pueden, por ejemplo, producirse reemplazando funcionalidades apropiadas presentes en los compuestos de la fórmula I con ciertos restos conocidos por los expertos en la técnica como 'pro - restos' como se describe, por ejemplo, en Design of Prodrugs por H. Bundgaard (Elsevier, 1985).

Algunos ejemplos de profármacos de acuerdo con la presente invención

incluyen, pero no se limitan a,

(i) cuando el compuesto de fórmula I contiene una funcionalidad ácido carboxílico (-COOH), un éster del mismo, por ejemplo, un compuesto en el que el hidrógeno de la funcionalidad ácido carboxílico del compuesto de la fórmula (I) se reemplaza por alquilo (C_1 - C_8);

(ii) cuando el compuesto de fórmula I contiene una funcionalidad alcohol (-OH), un éter del mismo, por ejemplo, un compuesto en el que el hidrógeno de la funcionalidad alcohol del compuesto de la fórmula I se reemplaza por alcanoil (C_1 - C_6) oximetilo; y

(iii) cuando el compuesto de fórmula I contiene una funcionalidad amino primaria o secundaria (-NH_2 o -NHR donde R ≠ H), una amida del mismo, por ejemplo, un compuesto en el que, como puede ser el caso, uno o ambos hidrógenos de la funcionalidad amino del compuesto de la fórmula I se reemplaza/n por alcanoílo (C_1 - C_{10}).

Los ejemplos adicionales de grupos de reemplazo de acuerdo con los ejemplos anteriores y ejemplos de otros tipos de profármacos se pueden encontrar en las referencias anteriormente mencionadas.

Además, ciertos compuestos de fórmula I pueden por ellos mismos actuar como profármacos de otros compuestos de fórmula I.

También incluidos dentro del ámbito de la invención están los metabolitos de los compuestos de fórmula I, esto es los compuestos formados *in vivo* tras la administración del fármaco. Algunos ejemplos de metabolitos de

acuerdo con la invención incluyen, pero no se limitan a,

(i) cuando el compuesto de fórmula I contiene un grupo metilo, un derivado hidroximetilo del mismo ($-CH_3$ -> $-CH_2OH$);

(ii) cuando el compuesto de fórmula I contiene un grupo alcoxi, un derivado hidroxi del mismo (-OR -> -OH);

(iii) cuando el compuesto de fórmula I contiene un grupo amino terciario, un derivado amino secundario del mismo ($-NR^1R^2$ -> $-NHR^1$ o $-NHR^2$);

(iv) cuando el compuesto de fórmula I contiene un grupo amino secundario, un derivado primario del mismo ($-NHR^1$ -> $-NH_2$):

(v) cuando el compuesto de fórmula I contiene un resto fenilo, un derivado fenol del mismo (-Ph -> -PhOH); y

(vi) cuando el compuesto de fórmula I contiene un grupo amida, un derivado ácido carboxílico del mismo ($-CONH_2$ -> -COOH).

Los compuestos de fórmula I que contienen uno o más átomos de carbonos asimétricos pueden existir en forma de dos o más estereoisómeros. Cuando un compuesto de fórmula I contiene un grupo alquenilo o alquenileno, son posibles los isómeros geométricos *cis/trasn* (o Z/E). Cuando los isómeros estructurales son interconvertibles mediante una barrera de baja energía, se puede producir isomería tautomérica ("tautomería"). Esto puede tomar la forma de tautomería de protón en compuestos de fórmula I que contienen, por ejemplo, un grupo imino, ceto, u oxima, o también la llamada tautomería de valencia en los compuestos que contienen un resto aromático. A esto sigue que un compuesto individual puede mostrar más de un tipo de isomería.

Incluidos dentro del ámbito de la presente invención están todos los

estereoisómeros, isómeros geométricos y formas tautómeras de los compuestos de fórmula I, que incluyen los compuestos que muestran más de un tipo de isomería, y las mezclas de uno o más de los mismos. También se incluyen las sales de adición de ácidos o básicas en las que el contraion es ópticamente activo, por ejemplo, *d*-lactato o *l*-lisina, o racémico, por ejemplo, *dl*-tartrato o *dl*-arginina.

Los isómeros *cis/trans* se pueden separar mediante técnicas convencionales bien conocidas por los expertos en la técnica, por ejemplo, cromatografía y cristalización fraccionada.

Las técnicas convencionales para la preparación/aislamiento de enantiómeros individuales incluyen síntesis quiral a partir de un precursor ópticamente puro adecuado o resolución del racemato (o el racemato de una sal o derivado) usando, por ejemplo, cromatografía líquida de alta presión quiral (HPLC).

Como alternativa, el racemato (o un precursor racémico) se puede hacer reaccionar con un compuesto ópticamente activo adecuado, por ejemplo, un alcohol, o, en el caso en el que el compuesto de la fórmula I contenga un resto ácido o base, una base o ácido tal como 1-feniletilamina o ácido tartárico. La mezcla diastereomérica resultante se puede separar mediante cromatografía y/o cristalización fraccionada y uno o ambos de los diastereoisómeros puede convertirse en el (los) correspondiente (s) entantiómero (s) puros mediante medios bien conocidos por los expertos en la técnica.

Los compuestos quirales de la invención (y precursores quirales de los mismos) se pueden obtener en forma enatioméricamente enriquecida usando cromatografía, típicamente HPLC, sobre una resina asimétrica con una fase

móvil constituida por un hidrocarburo, típicamente heptano o hexano, que contiene entre 0 y 50% en volumen de isopropanol, típicamente entre 2% y 20%, y entre 0 y 5% en volumen de una alquilamina, típicamente dietilamina al 0,1%. La concentración del eluato produce la mezcla enriquecida.

Cuando cualquier racemato cristaliza, son posibles cristales de dos tipos diferentes. El primer tipo es el compuesto racémico (verdadero racemato) mencionado anteriormente en el que se produce una forma homogénea de cristal que contiene ambos enantiómeros en cantidades equimolares. El segundo tipo es la mezcla racémica o conglomerado en el que se producen dos formas de cristal en cantidades equimolares cada una comprendiendo un enantiómero individual.

Aunque ambas formas cristalinas presentes en una mezcla racémica tienen propiedades físicas idénticas, pueden tener diferentes propiedades físicas comparadas con el verdadero racemato. Las mezclas racémicas se pueden separar mediante técnicas convencionales conocidas por los expertos en la técnica - véase, por ejemplo, Stereochemistry of Organic Compounds por E. L. Eliel y S. H. Wilen (Wiley, 1994).

La presente invención incluye todos los compuestos isotópicamente marcados farmacéuticamente aceptables de fórmula I en los que uno o más átomos se reemplazan por átomos que tienen el mismo número atómico, pero una masa atómica o número másico diferente de la masa atómica o número másico que predomina en la naturaleza.

Los ejemplos de isótopos adecuados para inclusión en los compuestos de la invención incluyen, pero no se limitan a, isótopos de hidrógeno, tal como ^{2}H y ^{3}H, carbono, tal como ^{11}C, ^{13}C y ^{14}C, cloro, tal como ^{36}Cl, flúor, tal como

^{18}F, yodo, tal como ^{123}I y ^{125}I, nitrógeno, tal como ^{13}N y ^{15}N, oxígeno, tal como ^{15}O, ^{17}O y ^{18}O, fósforo tal como ^{32}P, y azufre, tal como ^{35}S.

Ciertos compuestos marcados isotópicamente de fórmula I, por ejemplo, los que incorporan un isótopo radiactivo, son útiles en estudios de distribución en tejidos de fármacos y/o sustratos. Los isótopos radiactivos tritio, es decir, ^{3}H, y carbono - 14, es decir ^{14}C, son particularmente útiles para este propósito en vista de su fácil incorporación y fácil medio de detección.

La sustitución con isótopos más pesados tal como deuterio, es decir, ^{2}H, puede producir ciertas ventajas terapéuticas que se producen por una mayor estabilidad metabólica, por ejemplo, aumento de la semivida *in vivo* o reducción de los requerimientos de dosificación, y por lo tanto se puede preferir en algunas circunstancias.

La sustitución con isótopos que emiten positrones, tales como ^{11}C, ^{18}F, ^{15}O y ^{13}N, puede ser útil en los estudios de topografía de emisión de positrones (PET) para examinar la ocupación de receptores de sustratos.

Los compuestos marcados isotópicamente de fórmula I se pueden preparar generalmente mediante técnicas convencionales conocidas por los expertos en la técnica o mediante procedimientos análogos a los descritos en los ejemplos y preparaciones adjuntos usando un reactivo marcado isotópicamente apropiado en lugar del reactivo no marcado previamente empleado.

Los solvatos farmacéuticamente aceptables de acuerdo con la invención incluyen aquellos en los que el disolvente de cristalización puede estar sustituido isotópicamente, por ejemplo D_2O, d_6-acetona, d_6-DMSO.

Las realizaciones específicas de la presente invención incluyen los

compuestos ejemplificados en los ejemplos más adelante y las sales farmacéuticamente aceptables de los mismos, los complejos de los mismos, y los derivados de los mismos que se convierten en un compuesto farmacéuticamente activo tras la administración.

Los compuestos de la fórmula I de esta invención, y sus sales farmacéuticamente aceptables, tienen propiedades farmacéuticas y medicinales útiles. Los compuestos de fórmula I, y sus sales farmacéuticamente aceptables inhiben la producción de Aβ-péptido (así pues, actividad gamma-secretasa) en mamíferos, incluyendo seres humanos. Los compuestos de la fórmula I, y sus sales farmacéuticamente aceptables, son por lo tanto capaces de funcionar como agentes terapéuticos en el tratamiento de los trastornos y enfermedades neurodegenerativos y/o neurológicos enumerados representativamente más adelante, por ejemplo enfermedad de Alzheimer, en un mamífero afligido, incluyendo un ser humano.

La presente invención también se refiere a una composición farmacéutica para inhibir la producción de Aβ-péptidos en un mamífero, incluyendo un ser humano, que comprende una cantidad de un compuesto de la fórmula I, o una sal farmacéuticamente aceptable del mismo, que es eficaz en la inhibición de la Aβ-producción, y un vehículo farmacéuticamente aceptable.

La presente invención también se refiere a una composición farmacéutica para tratar una enfermedad o afección seleccionada entre el grupo constituido por enfermedad de Alzheimer, hemorragia cerebral hereditaria con amiloidosis, angiopatía amiloide cerebral, una enfermedad mediada por priones, miositis por cuerpos de inclusión, accidente

cerebrovascular, esclerosis múltiple, trauma cefálico, alteración cognitiva suave y síndrome de Down en un mamífero, incluyendo un ser humano, que comprende una cantidad de un compuesto de la fórmula I, o una sal farmacéuticamente aceptable del mismo, que es eficaz en la inhibición de la producción de Aβ- péptidos, y un vehículo farmacéuticamente aceptable.

La presente invención también se refiere a una composición farmacéutica para tratar una enfermedad o afección seleccionada entre el grupo constituido por enfermedad de Alzheimer y síndrome de Down en un mamífero, incluyendo un ser humano, que comprende una cantidad de un compuesto de la fórmula I, o una sal farmacéuticamente aceptable del mismo, que es eficaz en la inhibición de la producción de Aβ - péptidos, y un vehículo farmacéuticamente aceptable.

La presente invención también se refiere a una composición farmacéutica para tratar una enfermedad o afección seleccionada entre el grupo constituido por enfermedad de Alzheimer, hemorragia cerebral hereditaria con amiloidosis, angiopatía amiloide cerebral, una enfermedad mediada por priones, miositis por cuerpos de inclusión, accidente cerebrovascular, esclerosis múltiple, trauma cefálico, alteración cognitiva suave y síndrome de Down en un mamífero, incluyendo un ser humano, que comprende una cantidad de un compuesto de la fórmula I, o una sal farmacéuticamente aceptable del mismo, que es eficaz en el tratamiento de tal enfermedad o afección, y un vehículo farmacéuticamente aceptable.

La presente invención también se refiere a una composición farmacéutica para tratar una enfermedad o afección seleccionada entre el grupo constituido por enfermedad de Alzheimer y síndrome de Down en un

mamífero, incluyendo un ser humano, que comprende una cantidad de un compuesto de la fórmula I, o una sal farmacéuticamente aceptable del mismo, que es eficaz en el tratamiento de tal enfermedad o afección, y un vehículo farmacéuticamente aceptable.

La presente invención también se refiere a un procedimiento de inhibición de la producción de Aβ-péptidos en un mamífero, incluyendo un ser humano, que comprende la administración a dicho mamífero de una cantidad de un compuesto de la fórmula I, o una sal farmacéuticamente aceptable del mismo, que es eficaz en la inhibición de la Aβ-producción.

La presente invención también se refiere a un procedimiento de tratamiento de una enfermedad o afección seleccionada entre enfermedad de Alzheimer, hemorragia cerebral hereditaria con amiloidosis, angiopatía amiloide cerebral, una enfermedad mediada por priones, miositis por cuerpos de inclusión, accidente cerebrovascular, esclerosis múltiple, trauma cefálico, alteración cognitiva suave y síndrome de Down en un mamífero, incluyendo un ser humano, que comprende la administración a dicho mamífero de una cantidad de un compuesto de la fórmula I, o una sal farmacéuticamente aceptable del mismo, que es eficaz en la inhibición de la Aβ-producción.

La presente invención también se refiere a un procedimiento de tratamiento de una enfermedad o afección seleccionada entre enfermedad de Alzheimer y síndrome de Down en un mamífero, incluyendo un ser humano, que comprende la administración a dicho mamífero de una cantidad de un compuesto de la fórmula I, o una sal farmacéuticamente aceptable del mismo, que es eficaz en la inhibición de la Aβ-producción.

La presente invención también se refiere a un procedimiento de

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tratamiento de una enfermedad o afección seleccionada entre enfermedad de Alzheimer, hemorragia cerebral hereditaria con amiloidosis, angiopatía amiloide cerebral, una enfermedad mediada por priones, miositis por cuerpos de inclusión, accidente cerebrovascular, esclerosis múltiple, trauma cefálico, alteración cognitiva suave y síndrome de Down en un mamífero, incluyendo un ser humano, que comprende la administración a dicho mamífero de una cantidad de un compuesto de la fórmula I, o una sal farmacéuticamente aceptable del mismo, que es eficaz en el tratamiento de tal afección.

La presente invención también se refiere a un procedimiento de tratamiento de una enfermedad o afección seleccionada entre enfermedad de Alzheimer y síndrome de Down en un mamífero, incluyendo un ser humano, que comprende la administración a dicho mamífero de una cantidad de un compuesto de la fórmula I, o una sal farmacéuticamente aceptable del mismo, que es eficaz en el tratamiento de tal afección.

Los compuestos de fórmula I se pueden usar solos o usarse en combinación con cualquier otro fármaco, incluyendo, pero no se limitan a, cualquier agente potenciador de memoria, por ejemplo, Aricept ™ y/o Namenda ™, agente antidepresivo, por ejemplo, Zoloft ™, ansiolítico, agente antipsicótico, por ejemplo, Geodon ™, agente para el trastorno del sueño, agente anti - inflamatorio, por ejemplo, Celebrex ™, Bextra ™, etc., agente antioxidante, agente modulador de colesterol (por ejemplo, un agente que reduce LDL o incrementa HDL), por ejemplo, Lipitor ™, Caduet ™, etc., antagonista de Histamina (H2), por ejemplo, Cimetadina ™, y agente anti - hipertensivo, por ejemplo, Norvasc ™, Caduet ™, etc. De acuerdo a lo anterior, la presente invención también se refiere a las siguientes composiciones

farmacéuticas y procedimientos de tratamiento que comprenden un compuesto de la fórmula I en combinación con otros fármacos, tales como los del tipo descrito anteriormente.

La presente invención también se refiere a una composición farmacéutica para tratar una enfermedad o afección asociada a la producción de Aβ-péptidos en un mamífero, incluyendo un ser humano, que comprende (a) un compuesto de fórmula I, o una sal farmacéuticamente aceptable del mismo; (b) un agente potenciador de memoria, por ejemplo, Aricept ™ y/o Namenda ™, antidepresivo, por ejemplo, Zoloft ™, ansiolítico, agente antipsicótico, por ejemplo, Geodon ™, agente para el trastorno del sueño, agente anti - inflamatorio, por ejemplo, Celebrex ™, Bextra ™, etc., agente antioxidante, agente modulador de colesterol (por ejemplo, un agente que reduce LDL o incrementa HDL), por ejemplo, Lipitor ™, Caduet ™, etc., antagonista de Histamina (H2), por ejemplo, Cimetadina ™, y agente anti - hipertensivo, por ejemplo, Norvasc ™, Caduet ™, etc; y (c) un vehículo farmacéuticamente aceptable; en el que los agentes activos "a" y "b" anteriores están presentes en cantidades que hacen la composición eficaz en el tratamiento de tal enfermedad o afección.

La presente invención también se refiere a una composición farmacéutica para tratar una enfermedad o afección seleccionada entre el grupo constituido por enfermedad de Alzheimer, hemorragia cerebral hereditaria con amiloidosis, angiopatía amiloide cerebral, una enfermedad mediada por priones, miositis por cuerpos de inclusión, accidente cerebrovascular, esclerosis múltiple, trauma cefálico, alteración cognitiva suave y síndrome de Down en un mamífero, incluyendo un ser humano, que

comprende (a) un compuesto de fórmula I, o una sal farmacéuticamente aceptable del mismo; (b) un agente potenciador de memoria, por ejemplo, Aricept ™ y/o Namenda ™, antidepresivo, por ejemplo, Zoloft ™, ansiolítico, agente antipsicótico, por ejemplo, Geodon ™, agente para el trastorno del sueño, agente anti - inflamatorio, por ejemplo, Celebrex ™, Bextra ™, etc., agente antioxidante, agente modulador de colesterol (por ejemplo, un agente que reduce LDL o incrementa HDL), por ejemplo, Lipitor ™, Caduet ™, etc., antagonista de Histamina (H2), por ejemplo, Cimetadina ™, y agente anti - hipertensivo, por ejemplo, Norvasc ™, Caduet ™, etc; y (c) un vehículo farmacéuticamente aceptable; en el que los agentes activos "a" y "b" anteriores están presentes en cantidades que hacen la composición eficaz en el tratamiento de tal enfermedad o afección.

La presente invención también se refiere a una composición farmacéutica para tratar una enfermedad o afección seleccionada entre el grupo constituido por enfermedad de Alzheimer y síndrome de Down en un mamífero, incluyendo un ser humano, que comprende (a) un compuesto de fórmula I, o una sal farmacéuticamente aceptable del mismo; (b) un agente potenciador de memoria, por ejemplo, Aricept ™ y/o Namenda ™, antidepresivo, por ejemplo, Zoloft ™, ansiolítico, agente antipsicótico, por ejemplo, Geodon ™, agente para el trastorno del sueño, agente anti - inflamatorio, por ejemplo, Celebrex ™, Bextra ™, etc., agente antioxidante, agente modulador de colesterol (por ejemplo, un agente que reduce LDL o incrementa HDL), por ejemplo, Lipitor ™, Caduet ™, etc., antagonista de Histamina (H2), por ejemplo, Cimetadina ™, y agente anti - hipertensivo, por ejemplo, Norvasc ™, Caduet ™, etc; y (c) un vehículo farmacéuticamente

aceptable; en el que los agentes activos "a" y "b" anteriores están presentes en cantidades que hacen la composición eficaz en el tratamiento de tal enfermedad o afección.

La presente invención también se refiere a un procedimiento de tratamiento de una enfermedad o afección asociado con producción de Aβ-péptidos en un mamífero, incluyendo un ser humano, que comprende la administración a dicho mamífero de (a) un compuesto de fórmula I, o una sal farmacéuticamente aceptable del mismo; (b) un agente potenciador de memoria, por ejemplo, Aricept ™ y/o Namenda ™, antidepresivo, por ejemplo, Zoloft ™, ansiolítico, agente antipsicótico, por ejemplo, Geodon ™, agente para el trastorno del sueño, agente anti - inflamatorio, por ejemplo, Celebrex ™, Bextra ™, etc., agente antioxidante, agente modulador de colesterol (por ejemplo, un agente que reduce LDL o incrementa HDL), por ejemplo, Lipitor ™, Caduet ™, etc., antagonista de Histamina (H2), por ejemplo, Cimetadina ™, y agente anti - hipertensivo, por ejemplo, Norvasc ™, Caduet ™, etc; en el que los agentes activos "a" y "b" anteriores están presentes en cantidades que hacen la composición eficaz en el tratamiento de tal enfermedad o afección.

La presente invención también se refiere a un procedimiento de tratamiento de una enfermedad o afección seleccionada entre el grupo constituido por enfermedad de Alzheimer, hemorragia cerebral hereditaria con amiloidosis, angiopatía amiloide cerebral, una enfermedad mediada por priones, miositis por cuerpos de inclusión, accidente cerebrovascular, esclerosis múltiple, trauma cefálico, alteración cognitiva suave y síndrome de Down en un mamífero, incluyendo un ser humano, que comprende la administración a dicho mamífero de (a) un compuesto de fórmula I, o una sal

farmacéuticamente aceptable del mismo; y (b) un agente potenciador de memoria, por ejemplo, Aricept ™ y/o Namenda ™, antidepresivo, por ejemplo, Zoloft ™, ansiolítico, agente antipsicótico, por ejemplo, Geodon ™, agente para el trastorno del sueño, agente anti - inflamatorio, por ejemplo, Celebrex ™, Bextra ™, etc., agente antioxidante, agente modulador de colesterol (por ejemplo, un agente que reduce LDL o incrementa HDL), por ejemplo, Lipitor ™, Caduet ™, etc., antagonista de Histamina (H2), por ejemplo, Cimetadina ™, y agente anti - hipertensivo, por ejemplo, Norvasc ™, Caduet ™, etc; en el que los agentes activos "a" y "b" anteriores están presentes en cantidades que hacen la composición eficaz en el tratamiento de tal enfermedad o afección.

La presente invención también se refiere a un procedimiento de tratamiento de una enfermedad o afección seleccionada entre el grupo constituido por enfermedad de Alzheimer y síndrome de Down, en un mamífero, incluyendo un ser humano, que comprende la administración a dicho mamífero de (a) un compuesto de fórmula I, o una sal farmacéuticamente aceptable del mismo; (b) un agente potenciador de memoria, por ejemplo, Aricept ™ y/o Namenda ™, antidepresivo, por ejemplo, Zoloft ™, ansiolítico, agente antipsicótico, por ejemplo, Geodon ™, agente para el trastorno del sueño, agente anti - inflamatorio, por ejemplo, Celebrex ™, Bextra ™, etc., agente antioxidante, agente modulador de colesterol (por ejemplo, un agente que reduce LDL o incrementa HDL), por ejemplo, Lipitor ™, Caduet ™, etc., antagonista de Histamina (H2), por ejemplo, Cimetadina ™, y agente anti - hipertensivo, por ejemplo, Norvasc ™, Caduet ™, etc; en el que los agentes activos "a" y "b" anteriores están presentes en cantidades que hacen la composición eficaz en el tratamiento de tal enfermedad o afección.

Los compuestos de fórmula I, o cualquiera de las combinaciones descritas en los párrafos inmediatamente precedentes, se pueden opcionalmente usar junto con un inhibidor de la P-glicoproteína conocido, tal como verapamil.

Las referencias en esta memoria descriptiva a enfermedades y afecciones "asociadas a la producción de Aβ-péptidos" se refieren a las enfermedades o afecciones que se producen, al menos en parte, por Aβ-péptidos y/o la producción de los mismos. Así pues, el Aβ-péptido es un factor contribuyente, pero no necesariamente el único factor contribuyente, a "una enfermedad o afección asociada a la producción de Aβ-péptidos".

Los compuestos de fórmula I, o sus sales farmacéuticamente aceptables también se pueden usar para modular o inhibir la ruta de señalización de Notch en organismos, incluyendo seres humanos. La ruta de señalización de Notch es un mecanismo evolutivamente conservado utilizado por organismos, que varían entre gusanos y seres humanos, para regular la determinación del destino de diversos linajes celulares. Notch pertenece a la familia de los genes homeóticos del tipo del factor de crecimiento epidérmico, que codifica las proteínas transmembrana con números variables de repeticiones del tipo de factor de crecimiento epidérmico en el dominio extracelular. Existe una creciente evidencia de un papel de la ruta de Notch en las enfermedades humanas. Todos los componentes de la ruta se tienen que identificar todavía, pero entre los identificados hasta la fecha, las mutaciones que afectan a su interacción entre sí pueden conducir a una diversidad de síndromes y afecciones patológicas.

Por ejemplo, la señalización de Notch está típicamente asociada a la

decisión de predestinación de la célula. El hallazgo de que la activación de Notch estimula el crecimiento de capilares sugiere que los receptores de Notch se deben activar para permitir que este proceso se produzca. Por lo tanto, la modulación de Notch proporciona un procedimiento para regular la angiogénesis. Específicamente, la modulación de la señalización de Notch se puede usar para modular la angiogénesis (por ejemplo, bloqueo de la señalización de Notch para bloquear la angiogénesis). Esta inhibición de angiogénesis *in vivo* se puede usar como un medio terapéutico para tratar una diversidad de enfermedades, incluyendo pero sin limitación cáncer, retinopatía diabética, artritis reumatoide, psoriasis, enfermedad inflamatoria del intestino y arteriosclerosis.

La ruta de Notch también está implicada en el desarrollo y maduración de las células T, como se describe en Radtke, F. y col., Immunity 10: 547 - 558, 1999. Los compuestos de fórmula I, y sus sales farmacéuticamente aceptables son por lo tanto candidatos útiles para modular el sistema inmune, incluyendo el tratamiento de inflamación, asma, rechazo de injertos, enfermedad de injerto frente a huésped, enfermedad autoinmune y rechazo de transplantes.

Además, numerosos estudios publicados entre 2002 y 2004 han proporcionado evidencia convincente de que la señalización de Notch está frecuentemente elevada en una diversidad de tumores humanos (incluyendo, pero sin limitación a mama, próstata, páncreas y leucemia linfoblástica aguda de células T). Un estudio clave proporciona una fuerte asociación genética al papel de Notch en los tipos importantes de tumores. Específicamente, Weijzen y col., demostró que la señalización de Notch mantiene el fenotipo neoplásico

en las células transformadas Ras humanas. Weijzen y col., (2002) *Nature Med* 8: 979. Debido a que el 30% de las malignidades humanas pueden llevar mutaciones activadoras en al menos una de las tres isoformas de Ras, este hallazgo aumenta la posibilidad de que los inhibidores de Notch fueran una potente adición para la terapia anti - cáncer. Otros hallazgos de los estudios soportan un papel central de la señalización de Notch aberrante en la patogénesis de la leucemia/linfoma linfoblástica aguda de células T humanas. Pear y col., *Current Opinion in Hematology* (2004), 11 (6), 426 - 433.

De acuerdo a lo anterior, los compuestos de fórmula I, o sus sales farmacéuticamente aceptables, se pueden usar para tratar una enfermedad o afección seleccionada entre el grupo constituido por cáncer, arteriosclerosis, retinopatía diabética, artritis reumatoide, psoriasis, enfermedad inflamatoria del intestino, inflamación, asma, rechazo de injertos, enfermedad de injerto frente a huésped, enfermedad autoinmune y rechazo de transplantes.

Como se usa en esta memoria descriptiva, el término "tratando" se refiere a invertir, aliviar o inhibir el progreso de una enfermedad, trastorno o afección, o uno o más síntomas de tal enfermedad, trastorno o afección, a la que tal término se aplica. Como se usa en esta memoria descriptiva, "tratando" también se puede referir a la disminución de la probabilidad o incidencia de la aparición de una enfermedad, trastorno o afección en un mamífero comparado a una población control no tratada, o comparado con el mismo mamífero antes de tratamiento. Por ejemplo, como se usa en esta memoria descriptiva, "tratando" se puede referir a la prevención de una enfermedad, trastorno o afección, y puede incluir retraso o prevención de la aparición de una enfermedad, trastorno o afección, o retraso o prevención de los síntomas

asociados a una enfermedad, trastorno o afección. Como se usa en esta memoria descriptiva, "tratando" también se puede referir a la reducción de la gravedad de una enfermedad, trastorno o afección o los síntomas asociados a tal enfermedad, trastorno o afección antes de que el mamífero se vea aquejado con la enfermedad, trastorno o afección. Tal prevención o reducción de la gravedad de una enfermedad, trastorno o afección antes de la aflicción se refiere a la administración de la composición de la presente invención, como se describe en esta memoria descriptiva, a un sujeto que no está en el momento de administración aquejado con la enfermedad, trastorno o afección. Como se usa en esta memoria descriptiva "tratando" también se puede referir a la prevención de la recurrencia de una enfermedad, trastorno o afección o de uno o más síntomas asociados con tal enfermedad, trastorno o afección. Los términos "tratamiento" y "terapéuticamente", como se usan en esta memoria descriptiva, se refieren al acto de tratar tal como "tratar" se ha definido anteriormente.

Los compuestos de fórmula I, y sus sales farmacéuticamente aceptables, se pueden preparar como se describe en los esquemas de reacción y descripción siguientes. Salvo que se indique otra cosa, como se indica en los esquemas de reacción y descripción que siguen, R^1, R^2, R^3, R^4, R^6, R^7, R^8, R^9, R^{10}, R^{11}, A, Z y n son como se han definido anteriormente.

Los compuestos de fórmula I pueden tener átomos de carbono asimétricos y por lo tanto pueden existir en forma de mezclas racémicas, diastereómeros, o isómeros ópticos individuales.

La separación de una mezcla de isómeros de compuestos de fórmula I en isómeros individuales se puede llevar a cabo según los procedimientos

convencionales conocidos en la técnica.

Los compuestos de fórmula I se pueden preparar mediante los procedimientos descritos más adelante, junto con los procedimientos de síntesis conocidos en la técnica de la química orgánica, o las modificaciones y derivatizaciones que son familiares para los expertos en la técnica. Los procedimientos preferidos incluyen, pero no se limitan, a los descritos más adelante.

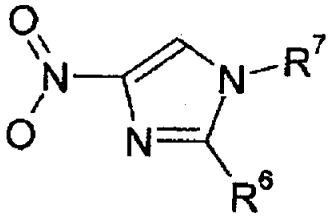
Las reacciones descritas más adelante se realizan en disolventes que son apropiados para los reactivos y materiales empleados y que son adecuados para uso en las reacciones descritas. En la descripción de los procedimientos sintéticos descritos más adelante, también se entiende que todas las condiciones de reacción, tanto reales como propuestas, incluyendo la elección del disolvente, temperatura de reacción, tiempo de duración de la reacción, presión de la reacción, y otras condiciones de la reacción (tales como condiciones anhidras, en argón, en nitrógeno, etc.), y procedimientos de tratamiento complementario, son condiciones que son las habituales para la reacción, como reconocerían fácilmente los expertos en la técnica. También se pueden usar procedimientos alternativos.

Los compuestos de la fórmula **II** en la que R^7 contiene un resto alcohol se pueden oxidar usando un procedimiento de oxidación convencional conocido en la técnica, tal como, por ejemplo, reactivos Dess - Martin, oxidación de Swern, o uso de SO_3-piridina, CrO_3, para proporcionar compuestos de fórmula **II** en la que R^7 contiene una cetona o aldehído. Los compuestos de fórmula **II** en la que R^7 es una cetona o aldehído se pueden convertir en los compuestos correspondientes de fórmula **II** en la que R^7 es una

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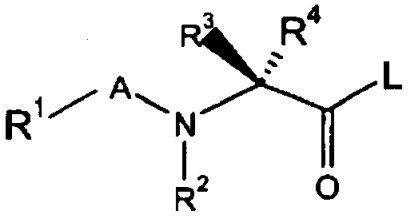
imina (mediante la reacción con una amina), olefina (mediante una reacción de Wittig), alcohol (mediante una reacción de Grignard), u otro derivado (mediante reacciones habituales).

Los compuestos de fórmula **I** de la presente invención y sus sales se pueden preparar mediante un procedimiento de reacción que comprende un compuesto de fórmula **II**.



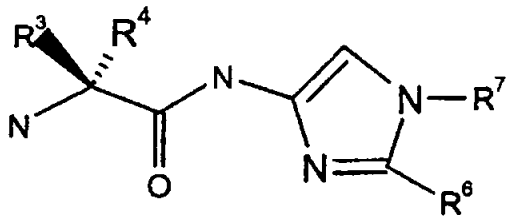
(II)

con un compuesto de fórmula **III**



(III)

o haciendo reaccionar un compuesto de fórmula **IV**



(IV)

con un compuesto de fórmula **V**



(V)

en la que R^1, R^3, R^4, R^6, R^7, y A son como se ha definido anteriormente y L es hidroxi o un grupo saliente adecuado. Si se desea, el derivado 4-amino-imidazol de fórmula **I** o un intermedio sintético de fórmula **IV** se puede convertir en una sal mediante procedimientos conocidos por los expertos en la técnica.

Los ejemplos de los compuestos específicos de fórmula **III** y **V** en las que L es hidroxi o un grupo saliente adecuado son aquellos en los que L representa un átomo de halógeno, tal como Cl, Br, o I, o A - L es un éster alquílico o arílico.

Los compuestos en la fórmula **I** se pueden preparar haciendo reaccionar un compuesto de fórmula II y un ácido carboxílico de fórmula **III**, o un compuesto de fórmula **IV** con un compuesto de fórmula **V**. Los compuestos de fórmula **IV** se pueden preparar haciendo reaccionar un compuesto de fórmula II con un compuesto de fórmula **VI**.

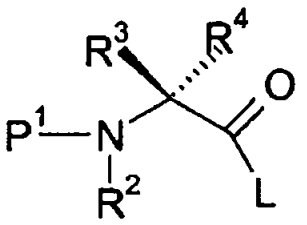
La reacción entre los compuestos de fórmula **II** y los compuestos de fórmula **III**, entre los compuestos de fórmula **IV** y los compuestos de fórmula **V**,

y entre los compuestos de fórmula **II** y los compuestos de fórmula **VI**, se pueden llevar a cabo mediante procedimientos habituales. Por ejemplo, cuando L es un grupo hidroxi, estas reacciones se pueden llevar a cabo en presencia de un agente de acoplamiento o un agente de acoplamiento soportado por un polímero, tal como, por ejemplo, carbodiimida, es decir 1,3-diciclohexilcarbodiimida (DCC), 1,3-diisopropilcarbodiimida, 1-(3-dimetilaminopropil)-3-etilcarbodiimida (EDC), N-ciclohexilcarbodiimida, o N'-metilpoliestireno en presencia o ausencia de HOBt, en un disolvente adecuado tal como, por ejemplo, un disolvente individual o una combinación de varios disolventes seleccionados entre diclorometano (CH_2Cl_2), cloroformo ($CHCl_3$), tetrahidrofurano (THF), éter dietílico (Et_2O), 1,4-dioxano, acetonitrilo, (CH_3CN), tolueno, N,N-dimetilformamida (DMF), o dimetilsulfóxido (DMSO), a una temperatura adecuada tal como entre aproximadamente -10ºC y aproximadamente reflujo, durante un tiempo adecuado controlado por cromatografía o CL - EM. Un procedimiento alternativo en el que L es OH se lleva a cabo convirtiendo OH en un grupo saliente mediante la reacción con cloruro de oxalilo, cloruro de tionilo o un procedimiento de mezcla de anhídridos, usando un cloroformiato de alquilo, tal como cloroformiato de alquilo C_1 - C_4, en presencia de una base tal como trietilamina, N,N-diisopropiletilamina, piridina, o dimetilaminopiridina, en un disolvente adecuado tal como, por ejemplo, cloruro de metileno, cloroformo, tetrahidrofurano (THF), tolueno, éter dietílico, acetonitrilo, 1,4-dioxano, N,N-dimetilformamida, dimetilsulfóxido (DMSO), N-metilpirrolidinona (NMP), o xileno, a una temperatura de entre aproximadamente -30ºC y aproximadamente temperatura ambiente.

Como alternativa, se puede lograr un acoplamiento de aminoimidazol como sigue. Un compuesto de fórmula **I** se puede preparar acoplando un aminoimidazol **II** con **III** en el que C(=O)L es un éster, en presencia de trialquilaluminio preferiblemente trimetilaluminio en un disolvente apropiado tal como cloruro de metileno, THF, dioxano, tolueno, etc., a una temperatura apropiada, tal como entre aproximadamente temperatura ambiente y aproximadamente temperatura de reflujo, o en un reactor sellado (tal como un tubo sellado o viales enroscados). De manera similar, el compuesto **IV** se puede preparar haciendo reaccionar un aminoimidazol **II**, triametilaluminio y N-Boc de un éster de alfa - aminoácido, seguido de la eliminación del grupo Boc usando procedimientos habituales.

Los compuestos amino protegidos de fórmula **VI**, en la que P^1 es un grupo bloqueante tal como un grupo N-Boc, se pueden preparar mediante procedimientos bien conocidos en la bibliografía, por ejemplo los procedimientos descritos en el libro de Theodora W. Greene "Protective Groups in Organic Synthesis". Los compuestos de fórmula **IV** se pueden preparar en un procedimiento análogo como se ha descrito anteriormente haciendo reaccionar un compuesto de fórmula **II** con un compuesto de fórmula **VI**; seguido del desbloqueamiento del grupo P^1. La desprotección se puede lograr mediante procedimientos bien conocidos, por ejemplo cuando P^1 es N-Boc, mediante eliminación mediante cualquier procedimiento bien conocido en la bibliografía, por ejemplo HCl(g) en un disolvente apropiado tal como 1,4-dioxano, dietiléter o ácido trifluoroacético en cloruro de metileno. Se conocen muchos otros grupos aminoprotectores y también se pueden usar, tales como bencilo o *p*-metoxibencilo, trimetilsililo, *t*-butildimetilsililo, etc. Los procedimientos para

desbloquear tales grupos también se conocen bien en la bibliografía y también se pueden usar.



(VI)

Los compuestos de fórmula **II, III, IV, V y VI**, en ciertas circunstancias, son compuestos conocidos o se pueden obtener según procedimientos bien conocidos por los expertos en la técnica.

Los compuestos de fórmula **III** y **V**, en las que L es un grupo saliente como se ha definido anteriormente, se pueden obtener según procedimientos convencionales a partir de los ácidos carboxílicos correspondientes de fórmula **III** en la que X es hidroxi.

Los compuestos de fórmula **IV** se pueden preparar haciendo reaccionar un compuesto de fórmula **II** con un compuesto de fórmula **V** usando procedimientos conocidos.

Un grupo éster de R^7 en los compuestos de fórmula **I** o **II** se puede convertir en la amida correspondiente usando un procedimiento similar para la formación de enlace amida, preferiblemente empleando trimetilaluminio en un disolvente apropiado o una mezcla de disolventes, tales como THF/tolueno.

Un grupo ceto de R^7 en los compuestos de fórmula **I** o **II** se puede convertir en la correspondiente amina usando un procedimiento de aminación

reductora bien establecido haciendo reaccionar tal cetona con una amina apropiada, con o sin catalizador ácido/acetato de amonio/agentes de secado (tales como Na_2SO_4 o $MgSO_4$ anhidros), y un agente reductor, tales como triacetoxi borohidruro de sodio, cianoborohidruro de sodio, o borohidruro de sodio, o los correspondientes $NaBH_4$ unido a polímero, $NaBH_3CN$ unido a polímero, o $NaB(OAc)_3H$ unido a polímero, o cualquier agente reductor (por ejemplo, hidrogenación) que se conoce en la bibliografía para reducir un enlace imina a una amina, en un disolvente apropiado, tal como dicloroetano, cloroformo, THF, MeOH, etanol, isopropanol, *t*-butanol o tolueno, a una temperatura entre aproximadamente temperatura ambiente y aproximadamente reflujo, preferiblemente entre aproximadamente temperatura ambiente y aproximadamente 65°C.

Los compuestos en los que R^6 es un grupo halo se pueden generar haciendo reaccionar el material de partida en el que R^6 es H con NBS (N-bromosuccinamida), NCS (N-clorosuccinamida), o SO_2Cl_2, I_2, en un disolvente apropiado tal como cloruro de metileno, tetracloruro de carbono o cloroformo. El grupo halo se puede después reemplazar con otro grupo usando procedimientos conocidos en la técnica, tal como intercambio halógeno - metal, seguido de la inactivación con un electrófilo, o usando condiciones de acoplamiento de Suzuki típicas que emplean un catalizador tal como un complejo de paladio, por ejemplo, tetrakis (trifenilfosfina)paladio, con carbonato de sodio como base, en un disolvente adecuado tal como THF, DME, o etanol, y un ácido bórico.

El 4-aminoimidazol **II** se puede preparar mediante los siguientes procedimientos conocidos en la bibliografía química (por ejemplo, Tetrahedron,

1995, 51, 2875 - 2894; J. Chem. Soc. Perkin 1, 1987, 2819 - 2828; Bull. Chem. Soc. Fr. 1994, 131, 200 - 209; Tetrahedron Lett. 1996, 4423 - 4426; Tetrahedron 1996, 37, 4423 - 4426; Tetrahedron, 1994, 50, 5741 - 5752; Heterocycles, 1994, 37, 1511 - 1520; Tetrahedron Lett, 1999, 1623 - 1626; Organic Lett. 2002, 4, 4133 - 4134; Organic Lett. 2000, 2, 1233 - 1236; J. Med. Chem. 1990, 33, 1091 - 1097; o mediante los procedimientos descritos más adelante.

El esquema 1 ilustra los procedimientos adecuados para preparar compuestos aminoimidazol de fórmula **I**. Con relación al esquema 1, el tratamiento de una solución de 1,4-dinitroimidazol (*J. Phys. Chem.*. (1995) Vol. 99, pp. 5009 - 5015) en dimetilsulfóxido (DMSO), piridina - agua, agua, un alcohol, o un sistema de disolventes alcohol - agua, pero preferiblemente en un alcohol inferior tal como metanol, entre aproximadamente -20°C y aproximadamente 50°C, preferiblemente entre aproximadamente -5°C y 35°C, con una alquil o aril amina primaria (NR^9R^{10}) produce 1-N-sustituido-4-nitroimidazoles de fórmula 2A. 1,4-Dinitroimidazol es una sustancia altamente energética, semiestable y se debe almacenar en un congelador siempre que no se use. Las mediciones termodinámicas han mostrado que puede generar potencialmente suficiente energía a 35°C en condiciones adiabáticas para explotar violentamente. Se debe ejercer precaución extrema siempre que se use este material. La reducción del compuesto nitro de fórmula **2A** a la amina de fórmula **3A** se puede llevar a cabo exponiendo una mezcla de un compuesto de fórmula **2A** y un catalizador de metal noble, en un disolvente tal como acetato de etilo, tetrahidrofurano, dioxano, o una mezcla de los mismos, a una atmósfera de gas hidrógeno a una presión de aproximadamente 1 a 100

atmósferas (101,325 a 10132,5 kPa), donde una presión preferida de gas hidrógeno está entre aproximadamente una y aproximadamente diez atmósferas (101,325 a 1013,25 kPa). Paladio es el catalizador de metal noble preferido. El metal se puede suspender convenientemente en un soporte sólido inerte tal como carbón y filtrarse para proporcionar la amina de fórmula **3A**. Como alternativa, la conversión del grupo nitro de fórmula **2A** a la amina de fórmula **3A** se puede lograr exponiendo una mezcla de un compuesto de fórmula **2A** a cinc/HCl o hierro/HCl o con $NaBH_4/NiCl_2$ o con $NaBH_2S_3$.

La amina resultante de fórmula **3A** se hace reaccionar inmediatamente con un cloruro de ácido, anhídrido de ácido, o un derivado de ácido carboxílico activado (definido por la fórmula **III**), en presencia de una base, tal como trietilamina, diisopropiletilamina, piridina, o 2,6-lutidina, entre aproximadamente -78°C y 40°C. La reacción entre compuestos de fórmula **3A** y los compuestos de fórmula **III** se puede llevar a cabo mediante procedimientos habituales. Por ejemplo, cuando L de fórmula **III** es un grupo hidroxi, estas reacciones se pueden llevar a cabo en presencia de un agente de acoplamiento o un agente de acoplamiento soportado por polímero, tal como por ejemplo, carbodiimida, es decir, 1,3-diciclohexilcarbodiimida (DCC), 1,3-diisopropilcarbodiimida, 1-(3-dimetilaminopropil)-3-etilcarbodimida (EDC), N-ciclohexilcarbodiimida, o N'-metilpoliestireno en presencia o ausencia de HOBt, en un disolvente adecuado tal como, por ejemplo, un disolvente individual o una combinación de varios disolventes seleccionados entre diclorometano (CH_2Cl_2), cloroformo ($CHCl_3$), tetrahidrofurano (THF), éter dietílico (Et_2O), 1,4-dioxano, acetonitrilo (CH_3CN), tolueno, N,N- dimetilformamida (DMF), o dimetilsulfóxido (DMSO), a una temperatura adecuada tal como entre aproximadamente -10°C y

aproximadamente reflujo, durante un tiempo adecuado controlado por cromatografía o CL - EM. Un procedimiento alternativo en el que L es OH se lleva a cabo convirtiendo OH en un grupo saliente mediante la reacción con cloruro de oxalilo, cloruro de tionilo o un procedimiento de mezcla de anhídrido, usando un cloroformiato de alquilo, tal como cloroformiato de alquilo C_1 - C_4, en presencia de una base tal como trietilamina, N,N-diisopropiletilamina, piridina, o dimetilaminopiridina, en un disolvente adecuado tal como, por ejemplo, cloruro de metileno, cloroformo, tetrahidrofurano (THF), tolueno, éter dietílico, acetonitrilo, 1,4-dioxano, N,N- dimetilformamida, dimetilsufóxido (DMSO), N-metilpirrolidinona (NMP), o xileno, a una temperatura de entre aproximadamente -30°C y aproximadamente temperatura ambiente.

Como alternativa, se puede lograr un acoplamiento de aminoimidazol como sigue. Un compuesto de fórmula **I** se puede preparar acoplando un aminoimidazol **3A** con un compuesto de fórmula **III** en el que C(=O)L es un éster, en presencia de trialquilaluminio preferiblemente trimetilaluminio en un disolvente apropiado tal como cloruro de metileno, THF, dioxano, tolueno, etc., a una temperatura apropiada, tal como entre aproximadamente temperatura ambiente y aproximadamente temperatura de reflujo, o en un reactor sellado (tal como un tubo sellado o viales enroscados).

Como alternativa, la amina resultante de fórmula **3A** se hace reaccionar inmediatamente con un cloruro de ácido, anhídrido de ácido, o un derivado de ácido carboxílico activado (definido por la fórmula **IV**), en presencia de una base, tal como trietilamina, diisopropiletilamina, piridina, o 2,6-lutidina, entre aproximadamente -78°C y 40°C para formar un compuesto de fórmula 4A. La reacción entre los compuestos de fórmula **3A** y los compuestos de fórmula **IV**

se puede llevar a cabo mediante procedimientos habituales. Por ejemplo, cuando L de fórmula **IV** es un grupo hidroxi, estas reacciones se pueden llevar a cabo en presencia de un agente de acoplamiento o un agente de acoplamiento soportado por polímero, tal como por ejemplo, carbodiimida, es decir, 1,3- diciclohexilcarbodiimida (DCC), 1,3-diisopropilcarbodiimida, 1-(3-dimetilaminopropil)-3-etilcarbodiimida (EDC), N-ciclohexilcarbodiimida, o N'-metilpoliestireno en presencia o ausencia de HOBt, en un disolvente adecuado tal como, por ejemplo, un disolvente individual o una combinación de varios disolventes seleccionados entre diclorometano (CH_2Cl_2), cloroformo ($CHCl_3$), tetrahidrofurano (THF), éter dietílico (Et_2O), 1,4-dioxano, acetonitrilo (CH_3CN), tolueno, N,N- dimetilformamida (DMF), o dimetilsulfóxido (DMSO), a una temperatura adecuada tal como entre aproximadamente -10°C y aproximadamente reflujo, durante un tiempo adecuado controlado por cromatografía o CL - EM. Un procedimiento alternativo en el que L es OH se lleva a cabo convirtiendo OH en un grupo saliente mediante la reacción con cloruro de oxalilo, cloruro de tionilo o un procedimiento de mezcla de anhídridos, usando un cloroformiato de alquilo, tal como cloroformiato de alquilo C_1 - C_4, en presencia de una base tal como trietilamina, N,N-diisopropiletilamina, piridina, o dimetilaminopiridina, en un disolvente adecuado tal como, por ejemplo, cloruro de metileno, cloroformo, tetrahidrofurano (THF), tolueno, éter dietílico, acetonitrilo, 1,4-dioxano, N,N- dimetilformamida, dimetilsulfóxido (DMSO), N-metilpirrolidinona (NMP), o xileno, a una temperatura de entre aproximadamente -30°C y aproximadamente temperatura ambiente.

Como alternativa, se puede lograr un acoplamiento de aminoimidazol

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como sigue. Un compuesto de fórmula **4A** se puede preparar acoplando un aminoimidazol **3A** con un compuesto de fórmula **IV** en el que C(=O)L es un éster, en presencia de trialquilaluminio preferiblemente trimetilaluminio en un disolvente apropiado tal como cloruro de metileno, THF, dioxano, tolueno, etc., a una temperatura apropiada, tal como entre aproximadamente temperatura ambiente y aproximadamente temperatura de reflujo, o en un reactor sellado (tal como un tubo sellado o viales enroscados). Los compuestos amino protegidos definidos como PG, tal como un compuesto con un grupo Boc, de fórmula **IV** se pueden preparar mediante procedimientos bien conocidos en la bibliografía, por ejemplo los procedimientos descritos en el libro de Theodora W. Greene "Protective Groups in Organic Synthesis".

Los compuestos definidos por la fórmula **5A** se pueden preparar a partir de los compuestos de fórmula **4A** desbloqueando el grupo PG. La desprotección se puede realizar mediante procedimientos bien conocidos, por ejemplo, cuando PG es N-Boc, por eliminación mediante cualquier procedimiento bien conocido en la bibliografía, por ejemplo HCl(g) en un disolvente apropiado tal como 1,4-dioxano, dietiléter o ácido trifluoroacético en cloruro de metileno. Se conocen muchos otros grupos amino protectores y también se pueden usar, tales como bencilo o *p*-metoxibencilo, trimetilsililo, *t*-butildimetilsililo, etc. Los procedimientos para desbloquear tales grupos se conocen bien en la bibliografía y también se pueden usar.

Los compuestos de la fórmula **I** se pueden formar mediante reacción entre compuestos de fórmula **5A** y los compuestos de fórmula **V** mediante procedimientos habituales. Por ejemplo, cuando L es un grupo hidroxi, estas reacciones se pueden llevar a cabo en presencia de un agente de

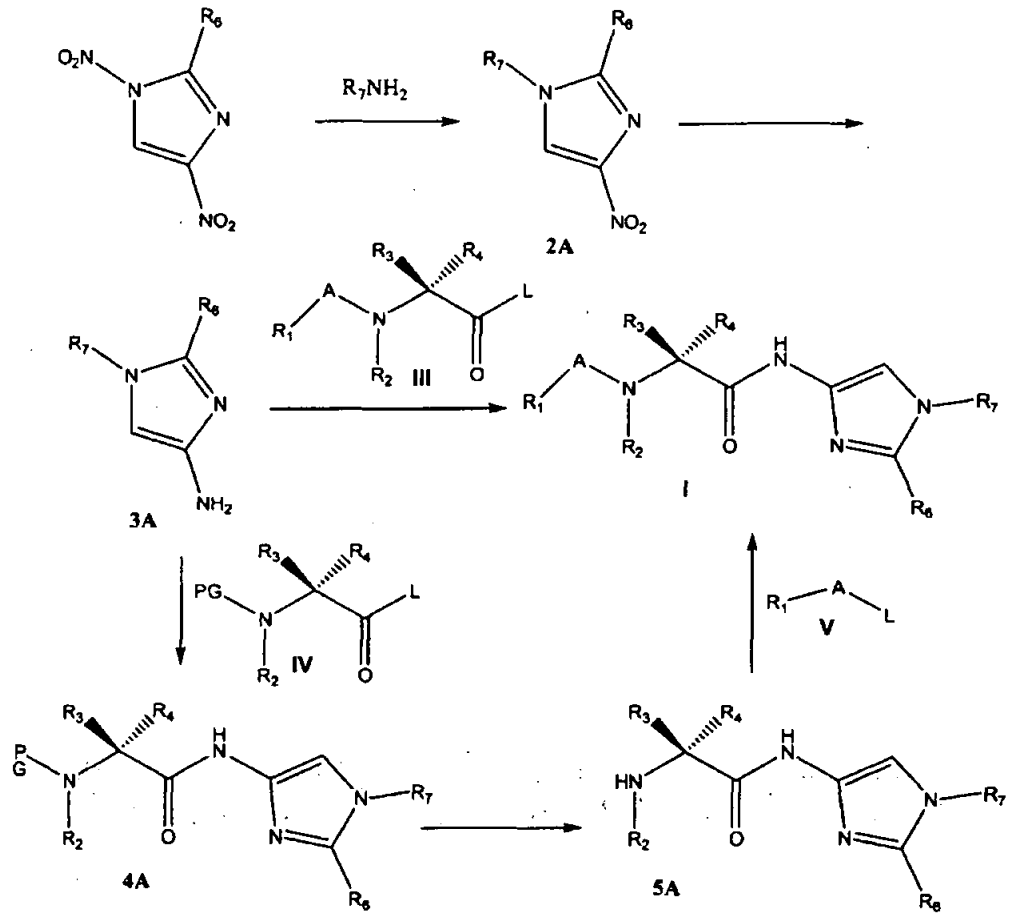
acoplamiento o un agente de acoplamiento soportado por polímeros, tal como por ejemplo, carbodiimida, es decir, 1,3-diciclohexilcarbodiimida (DCC), 1,3-diisopropilcarbodiimida, 1-(3-dimetilaminopropil)-3-etilcarbodiimida (EDC), N-ciclohexilcarbodiimida, o N'-metilpoliestireno en presencia o ausencia de HOBt, en un disolvente adecuado tal como, por ejemplo, un disolvente individual o una combinación de varios disolventes seleccionados entre diclorometano (CH_2Cl_2), cloroformo ($CHCl_3$), tetrahidrofurano (THF), éter dietílico (Et_2O), 1,4-dioxano, acetonitrilo (CH_3CN), tolueno, N,N-dimetilformamida(DMF), o dimetilsulfóxido (DMSO), a una temperatura adecuada tal como entre aproximadamente -10°C y aproximadamente reflujo, durante un tiempo adecuado controlado por cromatografía o CL - EM. Un procedimiento alternativo en el que L es OH se lleva a cabo convirtiendo OH en un grupo saliente mediante la reacción con cloruro de oxalilo, cloruro de tionilo o un procedimiento de mezcla de anhídridos, usando un cloroformiato de alquilo, tal como cloroformiato de alquilo C_1 - C_4, en presencia de una base tal como trietilamina, N,N-diisopropiletilamina, piridina, o dimetilaminopiridina, en un disolvente adecuado tal como, por ejemplo, cloruro de metileno, cloroformo, tetrahidrofurano (THF), tolueno, éter dietílico, acetonitrilo, 1,4-dioxano, N,N-dimetilformamida, dimetilsulfóxido (DMSO), N-metilpirrolidinona (NMP), o xileno, a una temperatura de entre aproximadamente -30°C y aproximadamente temperatura ambiente.

Como alternativa, se puede lograr un acoplamiento de aminoimidazol como sigue. Un compuesto de fórmula **I** se puede preparar acoplando un aminoimidazol **5A** con **V** donde L es un éster, en presencia de trialquilaluminio preferiblemente trimetilaluminio en un disolvente apropiado tal como cloruro de

metileno, THF, dioxano, tolueno, etc., a una temperatura apropiada, tal como entre aproximadamente temperatura ambiente y aproximadamente temperatura de reflujo, o en un reactor sellado (tal como tubo sellado o viales enroscados).

Como alternativa los compuestos de fórmula I se pueden formar mediante reacción entre los compuestos de fórmula **5A** y los compuestos de fórmula **V** donde L es un aldehído o cetona usando un procedimiento de aminación reductora bien establecido haciendo reaccionar tal cetona o aldehído con una amina apropiada **5A**, con o sin catalizador ácido/acetato de amonio/agentes de secado (tales como Na_2SO_4 o $MgSO_4$ anhidros), y un agente reductor, tales como triacetoxi borohidruro de sodio, cianoborohidruro de sodio, o borohidruro de sodio, o los correspondientes $NaBH_4$ unido a polímero, $NaBH_3CN$ unido a polímero, o $NaB(OAc)_3H$ unido a polímero, o cualquier agente reductor (por ejemplo, hidrogenación) que se conoce en la bibliografía para reducir un enlace imina a una amina, en un disolvente apropiado, tal como dicloroetano, cloroformo, THF, MeOH, etanol, isopropanol, *t*-butanol o tolueno, a una temperatura entre aproximadamente temperatura ambiente y aproximadamente reflujo, preferiblemente entre aproximadamente temperatura ambiente y aproximadamente 65°C.

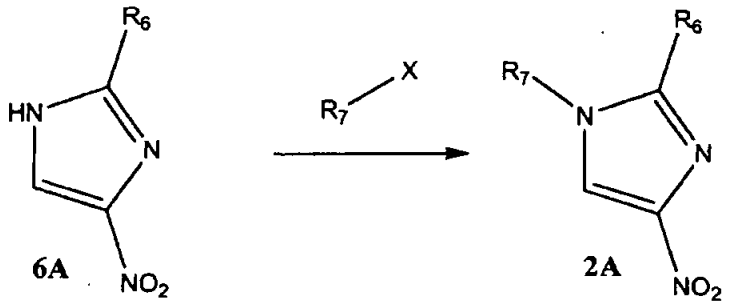
Esquema 1



El esquema 2 ilustra procedimientos adicionales para la síntesis de compuestos imidazol definidos por la fórmula **2A**. El tratamiento del *nitroimidazol* **6A** *con una base tal como hidruro de sodio, hidruro de potasio,* alquil litio, alcóxidos, en un disolvente tal como tetrahidrofurano, dimetilformamida, cloruro de metileno, éter, preferiblemente dimetilformamida, entre aproximadamente -60°C y 40°C, donde se prefiere entre -10°C y 20°C, seguido de la adición de R7-X en el que X se define como Cl, Br, I, F, alquilsulfonato, o arilsulfonato seguido de calentamiento de la reacción entre

23°C y 150°C donde se prefiere 30 - 80°C, produce imidazoles de fórmula **2A**. La reducción del compuesto nitro y reacción de acoplamiento se lleva a cabo de una manera similar a la descrita anteriormente y es útil para preparar los compuestos de fórmula I. Como alternativa, R7 se puede funcionalizar adicionalmente mediante procedimientos descritos en este documento o usando procedimientos conocidos por los expertos en la técnica.

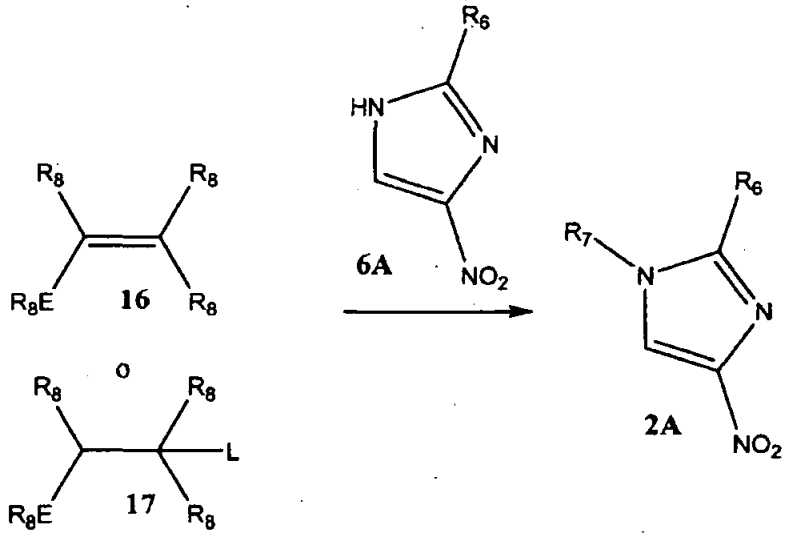
Esquema 2



El esquema 3 ilustra procedimientos adicionales para la síntesis de compuestos de nitroimidazol definidos por la fórmula **2A**. Un material de partida clave para la síntesis es el compuesto de doble enlace (un compuesto de fórmula **16** ó **17**) sustituido con el grupo ER8 y uno a tres grupos seleccionados entre R^8, donde ER8 se define como un grupo atractor de electrones elegido entre $C(=O)R^9$, $C(=O)OR^9$, $C(=O)NR^9R^{10}$, $S(=O)_2R^9$, $S(=O)_2NR^9R^{10}$, $S(=O)_2OR^9$, ciano, y heteroarilo. Adicionalmente, los compuestos de fórmula **16** ó **17** se pueden definir en los que ER8 se conecta a uno de los grupos R^8 o directamente al doble enlace carbono - carbono para formar un anillo y así incluye compuestos tales como 2-ciclopenteno-1-ona y 2-ciclohexeno-1-ona.

Como alternativa, los compuestos de fórmula **17** donde L se define como Cl, Br, I, $OC(=O)R^9$, o $OS(=O)_2R^9$ se pueden usar como materiales de partida; los ejemplos de tales compuestos son 3-cloro-1-ciclopentanona, 3-acetoxi-1-ciclobutanona. Así pues, con relación al esquema 3, el tratamiento de -= 4-nitroimidazol **6A**, con una base tal como hidruro de sodio, hidruro de potasio, carbonato de cesio, 1,8-diazabiciclo[5.4.0]undec-7-eno (DBU) o cloruro de tetraalquilamonio, donde DBU es la base preferida, con los intermedios **16** ó **17** en un disolvente tal como acetonitrilo, cloruro de metileno, 1,2-dicloroetano, o cloroformo, donde acetonitrilo es el disolvente preferido, a una temperatura entre aproximadamente -60°C y aproximadamente 50°C, donde -20°C a 23°C es el intervalo preferido, produce los productos de adición de fórmula **2A**. La reducción del compuesto nitro y el acoplamiento para dar los compuestos de fórmula I se lleva a cabo de una manera similar a la descrita anteriormente.

Esquema 3

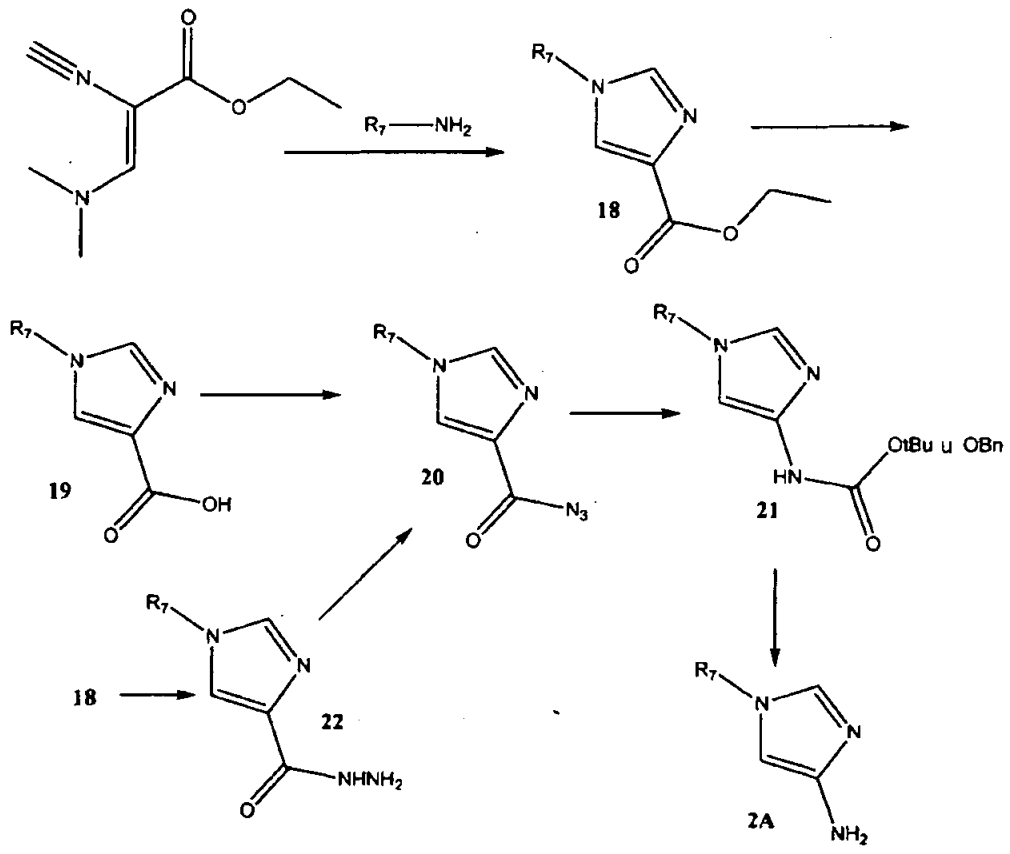


El esquema 4 más adelante ilustra procedimientos adicionales para la

síntesis de compuestos amino - imidazol definidos por la fórmula **2A**. El tratamiento de etil-2-isociano-3-*N,N*-dimetilamino acrilato o bencil-2-isociano-3-*N,N*-dimetilaminoacrilato con una amina primaria, R7-NH2, en un disolvente tal como *n*-butanol, *n*-propanol, *I*-propanol, o etanol, o en ausencia de disolvente, donde se prefiere *n*-propanol o ningún disolvente, entre aproximadamente 23°C y aproximadamente 200°C, donde se prefiere entre aproximadamente 60°C y 150°C, produce imidazoles de fórmula **18**. El tratamiento del éster **18** con una base tal como hidróxido de potasio, hidróxido de litio, o hidróxido de sodio en un disolvente tal como tetrahidrofurano, agua, metanol, etanol, propanol, en el que se prefiere metanol proporciona el ácido **19**. El ácido se convierte en la acilazida **20** usando los procedimientos conocidos por los expertos en la técnica tal como el tratamiento del ácido **19** con cloruro de tionilo o cloruro de oxalilo entre -20°C y 50°C seguido de la eliminación del disolvente residual e inactivando con azida de sodio o azida de potasio en un disolvente tal como tolueno, tetrahidrofurano, cloruro de metileno, dioxano. La azida **20** se somete a transposición de Curtis para obtener el Boc **21** mediante calentamiento entre 5°C y 200°C en un disolvente tal como *t*-butanol, alcohol bencílico, y etanol. Si se usa *t*-butanol, la desprotección del grupo protector N-Boc se puede llevar a cabo con HCl o ácido trifluoroacético en un disolvente tal como éter, tetrahidrofurano, donde se prefiere HCl en metanol, produce los compuestos aminoimidazol preferidos de fórmula **2A**. Si se usa alcohol bencílico, la desprotección se puede llevar a cabo mediante el uso de un catalizador de metal noble, en un disolvente tal como acetato de etilo, tetrahidrofurano, dioxano, o una mezcla de los mismos, en una atmósfera de gas hidrógeno a una presión de aproximadamente 1 a 100 atmósferas (101,325 - 10132,5 kPa),

donde una presión preferida de gas hidrógeno está entre aproximadamente una (101,325 kPa) y aproximadamente 10 atmósferas (1013,25 kPa) El catalizador de metal noble preferido es el paladio que produce los compuestos de aminoimidazol deseados de fórmula **2A**. Como alternativa, el éster **18** se puede tratar con hidracina en un disolvente tal como agua entre una temperatura de 50°C y 200°C donde se prefiere entre 80°C y 120°C y proporciona la hidrazida **22**. La hidrazida **22** se puede convertir en la acilazida **20** usando nitrito de *t*-butilo en un disolvente o combinación de disolventes tal como éter, cloruro de metileno, dicloroetano, cloroformo, donde se prefiere en éter/cloruro de metileno a una temperatura entre -50°C y 23°C donde se prefiere entre -30°C y 10°C. Después la acilazida se convierte en los compuestos de aminoimidazol de fórmula **2A** como se ha descrito anteriormente.

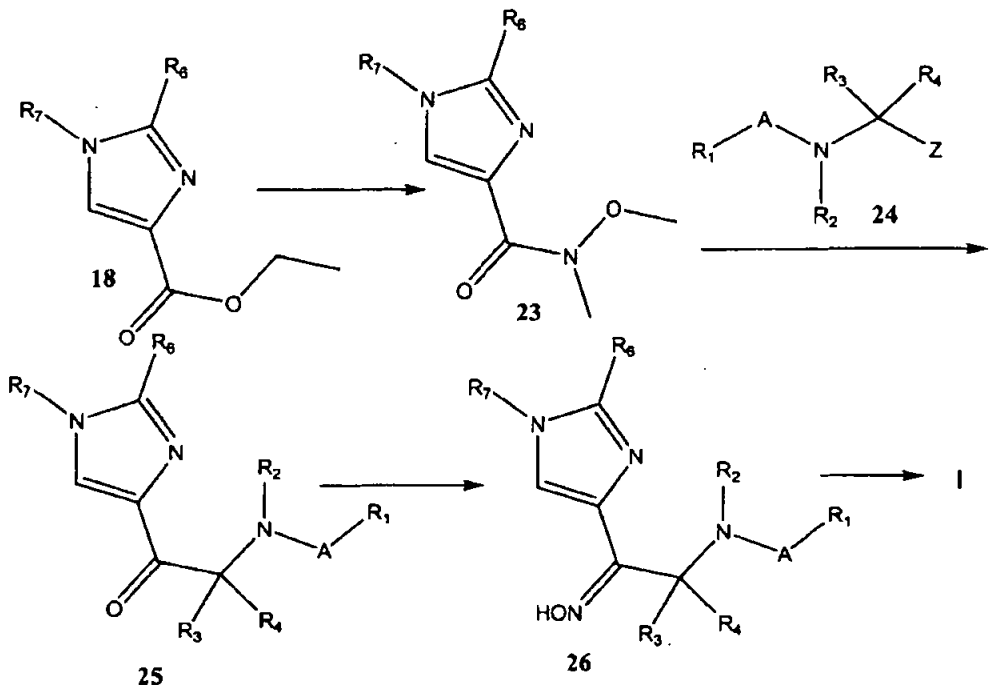
Esquema 4



El esquema 5 más adelante ilustra los procedimientos adicionales para la síntesis de compuestos de aminoimidazol definidos por la fórmula **I**. El tratamiento de clorhidrato de N,O-dimetilhidroxilamina con trimetilaluminio en 1,2- dicloroetano seguido de la adición del éster **18**, preparado como se ha descrito anteriormente y calentando a entre aproximadamente 30°C y aproximadamente 80°C, donde se prefiere una temperatura de aproximadamente 50°C, produce el imidazol **23**. La adición de un reactivo organometálico **24** en el que Z se define como haluro de litio, haluro de magnesio, haluro de potasio, donde se prefiere haluro de litio, a una solución

de la amida **23** en un disolvente tal como tetrahidrofurano, cloruro de metileno, o éter dietílico, entre una temperatura de aproximadamente -78°C y aproximadamente 30°C, donde se prefiere un intervalo de entre aproximadamente -20°C y aproximadamente 0°C produce **25**. La adición de **25** a una mezcla de clorhidrato de hidroxilamina y acetato de potasio en un disolvente de alcohol inferior donde se prefiere etanol, a aproximadamente 23°C, produce la oxima **26** en forma de una mezcla de isómeros. El tratamiento de una solución en acetona de la oxima **26** a aproximadamente 0°C con hidróxido acuoso seguido de cloruro de paratoluenosulfonilo produce una mezcla del compuesto de O-sulfonilo después de un tratamiento complementario de extracción. La disolución del material bruto en un disolvente no polar tal como benceno, hexanos, o tolueno, en el que se prefiere benceno, y la aplicación a una columna de alúmina seguido de elución con cloroformo - metanol (aproximadamente 10:1) después de aproximadamente cinco minutos proporciona un compuesto de fórmula **I**.

Esquema 5

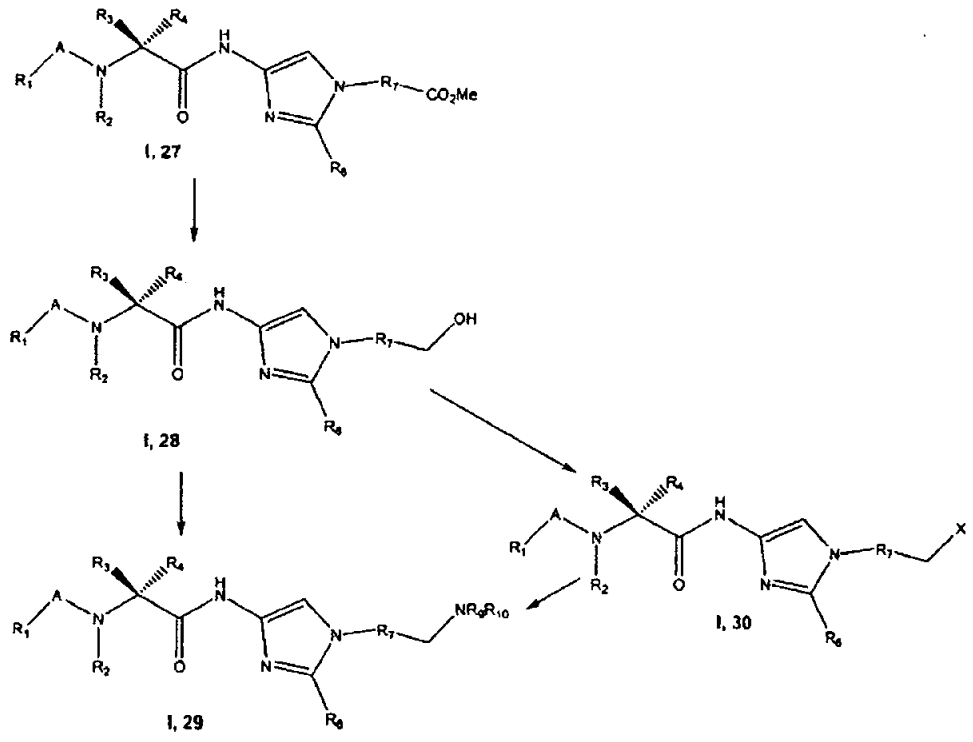


El esquema 6 ilustra procedimientos adecuados para preparar compuestos de aminoimidazol de la fórmula **I**. El compuesto de fórmula **I, 27** se puede preparar usando los procedimientos descritos anteriormente. La conversión de éster **I, 27** a alcohol de los compuestos **I, 28** se puede lograr mediante el tratamiento del éster **I, 27** con un agente reductor apropiado tal como bromuro sódico o hidruro de litio y aluminio usando condiciones bien conocidas para un experto en la técnica. Los compuestos de fórmula **I, 28**, se pueden oxidar usando un procedimiento de oxidación habitual conocido en la técnica, tal como, por ejemplo, reactivos de Dess - Martin, oxidación de Swern, o el uso de SO_3 - piridina, CrO_3, donde la oxidación de Swern se prefiere para proporcionar compuestos que contienen un aldehído. El aldehído se puede

convertir en los compuestos de fórmula **I, 29** usando un procedimiento de aminación reductora bien establecido haciendo reaccionar el aldehído con una amina **5A** apropiada, con o sin catalizador ácido/acetato de amonio/agentes de secado (tales como Na_2SO_4 o $MgSO_4$ anhidros), y un agente reductor, tal como triacetoxi borohidruro de sodio, cianoborohidruro de sodio, o borohidruro de sodio, o los correspondientes $NaBH_4$ unido a polímero, $NaBH_3CN$ unido a polímero, o $NaB(OAc)_3H$ unido a polímero, o cualquier agente reductor (por ejemplo, hidrogenación) que se conoce en la bibliografía para reducir un enlace imina a una amina, en un disolvente apropiado, tal como dicloroetano, cloroformo, THF, MeOH, etanol, isopropanol, *t*-butanol o tolueno, a una temperatura entre aproximadamente temperatura ambiente y aproximadamente reflujo, preferiblemente entre aproximadamente temperatura ambiente y aproximadamente 65°C. Como alternativa, el alcohol de **I, 28** se puede convertir en el correspondiente sulfonato de alquilo o arilo **I, 30** mediante tratamiento del alcohol con cloruro de alquilsulfonilo o de arilsulfonilo (donde se prefiere en cloruro de mesilo) en un disolvente tal como cloruro de metileno, tetrahidrofurano, tolueno donde se prefiere cloruro de metileno en presencia de una amina tal como trietilamina, diisopropilamina, piridina, 2,6-lutidina, donde se prefiere trietilamina a una temperatura entre -50°C y 23°C en la que se prefiere -0°C a 30°C. Después el sulfonato de arilo o alquilo se hace reaccionar con una azida de metal alcalino (en el que se prefiere azida de sodio), en un disolvente polar tal como dimetilformamida, dimetilsulfóxido, alcohol, en el que se prefiere etanol y produce un compuesto que contiene una azida. Esta azida intermedia se puede reducir mediante la exposición de la azida a un catalizador de metal noble, en un disolvente tal como acetato de etilo,

tetrahidrofurano, dioxano, o una mezcla de los mismos, en una atmósfera de gas hidrógeno a una pensión de aproximadamente 1 (101,325 kPa) a 100 atmósferas (10132,5 kPa), donde una presión preferida de gas hidrógeno es de aproximadamente 1 (101,325 kPa) a aproximadamente 10 atmósferas (1013,25 kPa). Paladio es el catalizador de metal noble preferido y la reacción produce el grupo amina. El grupo amina se puede después convertir en los compuestos de fórmula **1, 29** usando las condiciones de aminación reductora descritas anteriormente.

Esquema 6



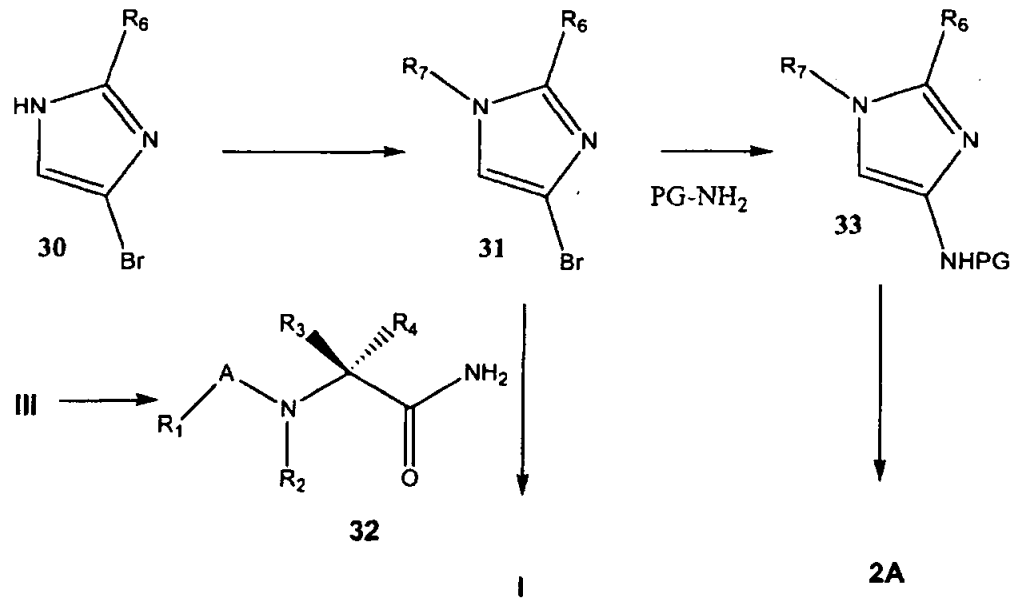
Con relación al esquema 7, el tratamiento de una solución de bromoimidazol **30** con una base, tal como hidruro de sodio, hidruro de potasio, hidruro de litio, carbonato de cesio, hidróxido de sodio, hidróxido de potasio,

hidróxido de cesio, diisopropilamiduro de litio, amiduro de sodio, hexametildisilazida de potasio, hexametildisilazida de sodio, *terc*-butóxido de sodio, o *terc*-butóxido de potasio, en un disolvente inerte de reacción tal como tetrahidrofurano, 1,4-dioxano, *N,N*-dimetilformamida, dimetilsulfóxido, o tolueno, entre aproximadamente -20°C y 150°C, donde se prefiere entre 20°C y 100°C, en la ausencia o presencia de un catalizador de transferencia de fase, tal como cloruro de *tetra-n*-butilamonio, bromuro de *tetra-n*-butilamonio, yoduro de *tetra-n*-butilamonio, cloruro de benciltrimetilamonio, bromuro de benciltrimetilamonio, o fluoruro de benciltrimetilamonio, seguido de la adición de un cloruro, bromuro, yoduro de alquilo, alilo, o bencilo, sulfonato de alquilo, sulfonato de arilo, o triflato, produce los imidazoles **31**.

El tratamiento de 1-sustituido-4-bromoimidazol (**31**) con un intermedio de fórmula **32** o PG-NH2 (donde PG se define como (C=O)alquilo o benzoílo) y un catalizador de paladio tal como acetato de paladio (II), dímero de cloruro de alilpaladio, tris(dibencilidenacetona)dipaladio (0), aducto de cloroformo de tris(dibencilidenacetona)dipaladio (0), o cloruro de paladio (II), donde acetato de paladio (II), tris(dibencilidenacetona)dipaladio (0), y aducto de cloroformo de tris(dibencilidenacetona)dipaladio (0) son los preferidos, y un ligando fosfina, preferiblemente 9,9-dimetil-4,5-bis(difenilfosfino)xanteno (XANTPHOS) se prefiere, y una base, tal como carbonato de cesio, o fosfato de potasio (K_3PO_4), donde se prefiere fosfato de potasio, en un disolvente inerte de reacción tal como tolueno, 1,4-dioxano, o tetrahidrofurano, entre aproximadamente 0°C y 150°C, donde se prefiere de 20°C a 110°C, produce el producto acoplado 1. Como alternativa, el tratamiento de 1-sustituido-4-bromoimidazol (**31**) con un intermedio de la fórmula **32** o PG- NH2 (donde PG se define como (C=O)alquilo

o benzoílo) y una diamina, tal como 1,2-etilendiamina, *N,N'*-dimetiletilendiamina, o cis-1,2-diaminociclohexano, preferiblemente *N,N'*-dimetiletilendiamina, y cloruro, bromuro o yoduro cuproso, preferiblemente yoduro cuproso, en presencia de una pequeña cantidad de agua, preferiblemente aproximadamente 1% a aproximadamente 4% de agua, en un disolvente inerte de reacción tal como 1,2-dimetoxietano, diglime, *t*-butilmetiléter, tetrahidrofurano, benceno o tolueno, preferiblemente tolueno, a una temperatura de aproximadamente 40°C a aproximadamente 150°C, preferiblemente aproximadamente 80°C a aproximadamente 120°C para producir el compuesto de fórmula **I** o los compuestos de fórmula **33**. En el caso del compuesto **33**, éste se puede convertir en los compuestos de fórmula **2A** usando los procedimientos convencionales descritos anteriormente.

Esquema 7



Los materiales de partida usados en los procedimientos de los esquemas anteriores, la síntesis de los cuales no se describe anteriormente,

están bien comercialmente disponibles, se conocen en la técnica o se obtienen fácilmente a partir de compuestos conocidos usando procedimientos que serán evidentes para los expertos en la técnica.

Los compuestos de fórmula I, y los intermedios mostrados en los esquemas de reacción anteriores, se pueden aislar y purificar mediante procedimientos convencionales, tales como recristalización o separación cromatográfica, tal como sobre gel de sílice, bien con un gradiente de elución de acetato de etilo/hexano, un gradiente de elución de cloruro de metileno/metanol, o un gradiente de elución de cloroformo/metanol. Como alternativa, se puede usar una técnica de separación de HPLC preparativa de fase inversa o de HPLC quiral.

En cada una de las reacciones descrita o ilustrada anteriormente, la presión no es crítica salvo que se indique otra cosa. Las presiones entre aproximadamente 0,5 atmósferas y aproximadamente 5 atmósferas (50,663 kPa a 506,63 kPa) son generalmente aceptables, y se prefiere presión ambiente, es decir, aproximadamente 1 atmósfera (101,325 kPa) como una cuestión de conveniencia.

Los compuestos de fórmula I de la presente invención son útiles en la inhibición de la producción de Aβ-péptidos (por lo tanto, actividad gamma - secretasa) en mamíferos, y por lo tanto son capaces de funcionar como agentes terapéuticos en el tratamiento de los trastornos y enfermedades anteriormente mencionados en un mamífero aquejado.

Un compuesto específico de la fórmula I se puede determinar para inhibir la producción de Aβ-péptidos usando ensayos biológicos conocidos por los expertos en la técnica, por ejemplo los ensayos descritos más adelante.

Para ensayar la eficacia *in vitro,* se determinó el efecto de los compuestos de ensayo en la secreción de Aβ desde las células en cultivo de tejidos. Se transfectaron de manera estable células H4 (neuroglioma de cerebro humano) con APP695 humano que contenía la mutación de la enfermedad de Alzheimer familiar sueca. Las células se distribuyeron en placas de 96 pocillos a una densidad de aproximadamente 30.000 células/pocillo y se dejó unir a la superficie de la placa durante aproximadamente 6 horas a 37°C. Después de este tiempo, se lavaron las células para retirar Aβ secretado y se añadió medio reciente que contenía el compuesto de ensayo. Después de la incubación con el compuesto durante toda una noche a 37°C, se recogió el medio y se sometió a inmunoensayo para determinar la cantidad de Aβ secretado desde las células. Se pueden aplicar a estas muestras diversos ensayos para los péptidos Aβ conocidos por los expertos en la técnica para cuantificación de la secreción de Aβ. En esta solicitud, los inventores utilizaron un ELISA de sándwich de dos sitios que utiliza anticuerpos monoclonales comercialmente disponibles, 6E10 y 4G8-biotinilado para proporcionar una estimación de la cantidad de la mayoría de las formas fisiológicamente relevantes de Aβ, por ejemplo, Aβ 1-40, Aβ1-42. Las señales de estas muestras se compararon con las curvas patrones generadas con péptido Aβ1-40 sintético y se usaron para calcular los valores de CI_{50} para cada compuesto de ensayo.

Usando tal ensayo, los compuestos de la presente invención se determinó que tenían una actividad CI_{50} para inhibir la actividad gamma secretasa de menos de aproximadamente 800 micromolar. Los compuestos preferidos de la invención son compuestos que se determinó que tenían una

actividad CI_{50} para inhibir la actividad gamma - secretasa de menos que aproximadamente 1 micromolar.

Los siguientes ejemplos ilustran la presente invención. Sin embargo, se debe entender que la invención, como se describe en esta memoria descriptiva y como se indica en las reivindicaciones, no se pretende que esté limitada por los detalles de los siguientes ejemplos.

Ejemplos

Procedimiento general A:

Procedimiento de acoplamiento para formación de amidas

a) Procedimiento de acoplamiento con EDC/HOBt/trialquilamina

Una mezcla de un ácido carboxílico (1,0 eq.), amina (1,0 eq.), HOBt (1,1 - 1,5 eq.) EDC (1,2 - 1,8 eq.) y una trialquilamina (trietilamina o diisopropiletilamina) (3 - 6 eq.) en un disolvente apropiado o una mezcla de disolventes, por ejemplo cloruro de metileno, dicloroetano, THF, o DMF, se agitó a temperatura ambiente hasta la formación de producto o desaparición del material de partida. El disolvente se retiró a presión reducida, el residuo se recogió en acetato de etilo (o disolvente seleccionado similar tal como cloruro de metileno o cloroformo) y agua. Se separó la fase orgánica, se lavó con HCl diluido (si el producto deseado contiene un grupo funcional básico, el lavado con HCl diluido se puede omitir), salmuera, y se secó sobre sulfato sódico. Después el disolvente se retiró a presión reducida proporcionando el producto.

b) Procedimiento de acoplamiento con HATU/trialquilamina

Una mezcla de un ácido carboxílico (1,0 eq.), amina (1,0 eq.), HATU (1,1 - 1,5 eq.) y una trialquilamina (trietilamina o diisopropiletilamina) (3 - 6 eq.)

en un disolvente apropiado o una mezcla de disolventes, por ejemplo cloruro de metileno, dicloroetano, THF, o DMF, se agitó a temperatura ambiente hasta la formación de producto o desaparición del material de partida. El disolvente se retiró a presión reducida, el residuo se recoge en acetato de etilo (o disolvente seleccionado similar tal como cloruro de metileno o cloroformo) y agua. Se separó la fase orgánica, se lavó con HCl diluido (si el producto deseado contiene un grupo funcional básico, el lavado con HCl diluido se puede omitir), salmuera, y se seca sobre sulfato sódico. Después el disolvente se retiró a presión reducida proporcionando el producto.

c) Procedimiento de acoplamiento con PyBOP/trialquilamina

Una mezcla de un ácido carboxílico (1,0 eq.), amina (1,0 eq.), PyBOP (1,1 - 1,5 eq.) y una trialquilamina (trietilamina o diisopropiletilamina) (3 - 6 eq.) en un disolvente apropiado o una mezcla de disolventes, por ejemplo cloruro de metileno, dicloroetano, THF, o DMF, se agitó a temperatura ambiente hasta la formación de producto o desaparición del material de partida. El disolvente se retiró a presión reducida, el residuo se recogió en acetato de etilo (o disolvente seleccionado similar tal como cloruro de metileno o cloroformo) y agua. Se separó la fase orgánica, se lavó con HCl diluido (si el producto deseado contiene un grupo funcional básico, el lavado con HCl diluido se puede omitir), salmuera, y se secó sobre sulfato sódico. Después el disolvente se retiró a presión reducida proporcionando el producto.

d) Procedimiento de acoplamiento con HBTU/trialquilamina

Una mezcla de un ácido carboxílico (1,0 eq.), amina (1,0 eq.), HBTU (1,1 - 1,5 eq.) y una trialquilamina (trietilamina o diisopropiletilamina) (3 - 6 eq.) en un disolvente apropiado o una mezcla de disolventes, por ejemplo cloruro de

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metileno, dicloroetano, THF, o DMF, se agitó a temperatura ambiente hasta la formación de producto o desaparición del material de partida. El disolvente se retiró a presión reducida, el residuo se recogió en acetato de etilo (o disolvente seleccionado similar tal como cloruro de metileno o cloroformo) y agua. Se separó la fase orgánica, se lavó con HCl diluido (si el producto deseado contiene un grupo funcional básico, el lavado con HCl diluido se puede omitir), salmuera, y se secó sobre sulfato sódico. Después el disolvente se retiró a presión reducida proporcionando el producto.

e) Procedimiento de acoplamiento con cloro - alquilformiato

Una mezcla de un ácido carboxílico (1,0 eq.) y trietilamina (eq.) se disolvió en un disolvente apropiado tal como DMF y se enfrió hasta -23°C. Se añadió gota a gota formiato de *iso*-butilo (1 eq.) con agitación. Después de agitar durante un período de tiempo (entre 15 minutos y 2 horas), se añadió un 2-aminotiazol o una amina (1 eq.) y se continuó la agitación durante 30 minutos adicionales a -23°C. Después la mezcla se calentó hasta temperatura ambiente hasta la formación de amida (típicamente toda una noche). La mezcla se inactivó con agua y salmuera y se extrajo con un disolvente apropiado tal como adetato de etilo, cloruro de metileno o cloroformo. La fase orgánica se lavó con $NaHSO_4$ diluido, $NaHCO_3$ y salmuera y se retiró el disolvente a presión reducida proporcionando el producto. Puede ser necesaria purificación.

f) Procedimiento de acoplamiento con TPTU

Al ácido (1 equiv.) suspendido en DMF seca, se añadieron diisopropiletilamina (2 - 4 equiv.) y TPTU (1 equiv.) y la mezcla resultante se agitó a temperatura ambiente durante 1 a 2 horas. A una alícuota de esta solución se añadió la amina apropiada y la mezcla se agitó a temperatura

ambiente durante toda una noche. Se añadió NaOH 1 N y la mezcla resultante se extrajo con acetato de etilo. Los extractos orgánicos se cargaron en un cartucho SCX SPE (Siliciclo, 1 g) que se lavó con MeOH. Después el producto se eluyó con trietil amina 1 N en MeOH y se concentró la fracción resultante. La purificación se hizo sobre una columna Waters XTerra PrepsMS C18 OBD (19 x 100 mm) y proporcionó el compuesto del título. Gradiente de elución con agua / acetonitrilo (18 ml/min) con modificador ácido trifluoroacético al 1% (2 ml/min).

Procedimiento general B:

Procedimiento para aminación reductora

a) Triacetoxiborohidruro de sodio

Una amina (1 - 4 eq.) en dicloroetano o THF se añadió a una solución de una cetona (1 eq.), $NaBH(OAc)_3$ (1 - 3 eq.) y ácido acético (1 - 3 eq.) en dicloroetano o THF. La mezcla se agitó a temperatura ambiente hasta la formación de producto o desaparición del material de partida. La mezcla se inactivó con base diluida, se extrajo con cloruro de metileno u otro disolvente apropiado tal como cloroformo o acetato de etilo. Se separó la fase orgánica, se secó y se concentró proporcionando la amida deseada. Puede ser necesaria purificación.

b) Cianoborohidruro de sodio

Una mezcla de una cetona o aldehído (1 eq.), una amina (1 - 20 eq.), cianoborohidruro de sodio (1 - 5 eq.), ácido acético (1 - 3 eq.), acetato de sodio (1 - 3 eq.), sulfato sódico anhidro en dicloroetano o THF se agitó a temperatura ambiente hasta 60°C, preferiblemente se calentó a 35 - 50°C hasta la formación de producto. La mezcla se inactivó con base diluida, se extrajo con cloruro de

metileno u otro disolvente apropiado tal como cloroformo o acetato de etilo. Se separó la fase orgánica, se secó y se concentró proporcionando la amida deseada. Puede ser necesaria purificación.

c) Formiato de potasio y acetato de paladio

Una solución de un aldehído o una cetona (1 eq.) y una amina (1 eq.) en DMF seca se agitó a temperatura ambiente durante 4 horas, en presencia de tamices moleculares. A la mezcla de reacción resultante se añadieron formiato de potasio (2 eq.) y acetato de paladio (cantidad catalítica, 0,02 eq.). La mezcla se calentó a 40 - 60°C hasta que se completó la reacción (TLC) y después de enfriar se diluyó con agua de hielo. La mezcla se extrajo con disolvente apropiado (tal como cloruro de metileno, acetato de etilo, o cloroformo). La fase orgánica se separó, se secó y se concentró proporcionando la amida deseada. Puede ser necesaria purificación.

Procedimiento general C:

Reducción de cetona o aldehído con borohidruro de sodio

Una mezcla de un aldehído o cetona (1 eq.) y borohidruro de sodio (1 - 10 eq.) en un disolvente apropiado (metanol o etanol) se agitó a 0°C hasta temperatura ambiente durante 10 minutos hasta que se completa la reacción (TLC). La mezcla se concentró hasta un pequeño volumen, se inactivó con agua, se extrajo con un disolvente apropiado (tal como cloruro de metileno, acetato de etilo, o cloroformo). La fase orgánica se separó, se secó y se concentró proporcionando la amida deseada. Puede ser necesaria purificación.

Procedimiento general D:

Procedimiento de desprotección de N-tBOC

A una solución de compuesto N-tBOC en 1,4-dioxano (0,03 - 0,09 M) se

añadió HCl 4 N en 1,4 dioxano o gas HCl anhidro en nitrógeno. La mezcla de reacción se agitó a temperatura ambiente durante 1 - 24 horas hasta que se consumió todo el material de partida (TLC). La solución se concentró y se bombeó en vacío. La sal final de HCl de la correspondiente amina se usó típicamente sin purificación adicional.

Procedimiento general E:

Adición conjugada a nitroimidazol

A una suspensión de 4-nitroimidazol (2,0 eq.) en acetonitrilo se añade DBU (1,0 equiv.) seguido de enona (1,0 equiv.). La reacción se calienta durante 12 - 24 horas y el disolvente se retira a vacío. Los sólidos resultantes se retiran mediante filtración con cloruro de metileno y el aceite resultante se concentra y se purifica mediante cromatografía sobre gel de sílice proporcionando el nitroimidazol deseado.

Procedimiento general F:

Alquilación de nitroimidazol usando hidruro sódico

A una suspensión de 4-nitroimidazol (1,0 eq.) en dimetilformamida a TA en atmósfera de nitrógeno se añade hidruro de sodio (1,2 equiv.) por partes. La reacción se agita durante 15 - 30 minutos. Y después se añade el haluro de alquilo o mesilato de alquilo adecuado. La mezcla se agita durante 12 - 24 horas a 50°C, se enfría a 0°C, y se inactiva con agua. La fase acuosa se extrae con cloruro de metileno, se seca, y se purifica mediante cromatografía sobre gel de sílice proporcionando el nitroimidazol deseado.

Alquilación de nitroimidazol usando carbonato potásico

A una suspensión de 4-nitroimidazol (1,0 eq.) en dimetilformamida a temperatura ambiente en una atmósfera de nitrógeno se añade carbonato

potásico (1 - 4 equiv) por partes. La reacción se agita durante 15 - 30 minutos. Y después se añade el haluro de alquilo o mesilato de alquilo apropiado. La mezcla se agita durante 12 - 24 h a 50°C a 90°C, se enfría a T A, y se inactiva con agua. La fase acuosa se extrae con cloruro de metileno, se seca y se purifica mediante cromatografía sobre gel de sílice o se recristaliza proporcionando el nitroimidazol deseado.

Procedimiento general G:

Reducción de nitroimidazol A

A una solución del nitroimidazol (1,0 eq.) en acetato de etilo se añade paladio sobre carbono (0,25 % en p/p). La reacción se hidrogena @ 40 - 60 psi (275,86 kPa - 413,79 kPa) durante 2 - 6 horas y se filtra sobre una capa de celita usando acetato de etilo. La mayoría de acetato de etilo se retira a vacío y la solución de la amina en el acetato de etilo restante se usa sin posterior purificación.

Reducción de nitroimidazol B

Se cargó una botella Parr con nitroimidazol (1 equiv.), dioxano, y (1 - 3 equiv) de níquel Raney que se había lavado con agua hasta que el sobrenadante estaba a pH = 7. La mezcla se colocó a 50 psi (344,83 kPa) de presión de hidrógeno y se agitó durante 45 minutos. Después de la filtración y evaporación, el producto se usó directamente en la siguiente etapa sin purificación adicional.

Procedimiento general H:

Reducción de éster de nitroimidazol seguido de aminación reductora

A una solución de éster apropiado tal como el éster metílico del ácido 3-metil-3-(4-nitroimidazol-1-il)butírico (1,0 equiv.) en cloruro de metileno a -78°C

se añade gota a gota DIBAL (2 equiv.). La reacción se agita durante 1 hora, se inactiva con acetato de etilo, se retira del baño de enfriamiento, y se agita durante 10 minutos. A la reacción se añade agua y se deja calentar hasta T A y se agita durante 1 hora. La reacción se diluye con cloruro de metileno, se añade Na_2SO_4 y la reacción se filtra a través de celita. El disolvente se retira proporcionando el aldehído 2-metil-2-(4- nitroimidazol-1-il)propionaldehído que se usa en la siguiente etapa sin purificación adicional.

A una solución del aldehído apropiado tal como 2-metil-2-(4-nitroimidazol-1-il)-propionaldehído (1 equiv.) en cloruro de metileno se añade una amina apropiada (2 equiv.) y tamices moleculares de 4 A. La reacción se agita durante 4 - 6 y se añade un agente de reducción tipo hidruro apropiado tal como triacetoxiborohidruro de sodio (2 equiv.). La reacción se agita durante 6 - 24 horas, se inactivó con bicarbonato sódico, y la fase acuosa se extrae con cloruro de metileno. Se retira el disolvente y se purifica el residuo mediante cromatografía sobre gel de sílice proporcionando el nitroimidazol deseado.

Procedimiento General I

Reducción del éster

A una solución del éster (1 equiv.) en un disolvente apropiado tal como éter dietílico o tetrahidrofurano a -78°C a 0°C se añade hidruro de litio y aluminio (1 equiv.) y la reacción se agita a 0°C durante 15 minutos y se calienta a T A durante 1 hora. La reacción se inactiva lentamente con agua y acetato de etilo. La reacción se filtra y la fase acuosa se extrae con acetato de etilo, se seca, y se concentra. Como alternativa, la reacción se inactiva con agua, NaOH 1 N y agua, se agita y se filtra a través de Celita. El filtrado se concentra hasta sequedad.

Usando cualquier tratamiento, el residuo resultante se purifica mediante cromatografía de gel de sílice proporcionando el alcohol del título.

Procedimiento general J

Oxidación de Swern

A una solución de cloruro de oxalilo (1,2 equiv.) en cloruro de metileno a -78°C se añade DMSO (3 equiv) gota a gota. La reacción se agita durante 20 minutos y se añade el alcohol (1 equiv) en cloruro de metileno. La reacción se agita durante 1 hora, se añade trietilamina (4 - 5 equiv), y la reacción se calienta a 0°C durante 20 minutos a 2 horas. La reacción se inactiva con 100 ml de bicarbonato sódico, se extrae con cloruro de metileno, se seca, y se concentra produciendo el compuesto del título.

Oxidación de Dess Martin

Una mezcla de 1 eq. de un alcohol y 1 a 1,5 eq. de agente de oxidación de Dess - Martin en cloruro de metileno (2 ml por mmol de reacción) se agitó a temperatura ambiente hasta que se realizó la reacción. La mezcla se inactivó con agua, se filtró. La fase orgánica se separó, se secó y se concentró proporcionando el aldehído correspondiente.

Procedimiento general K:

Apertura de epóxido

Se añadió isopropanol a la amina apropiada seguido de la adición de base de Hunig (2 equiv.) y el epóxido apropiado (1 equiv.), la mezcla de reacción se calentó a 60 - 100°C durante toda una noche. La mezcla se inactivó con solución acuosa diluida de bicarbonato y se extrajo con diclorometano. Se secaron los extractos orgánicos (Na_2SO_4) y se concentraron

produciendo 200 mg de material bruto que se purificó sobre una columna ultrarrápida de gel de sílice produciendo el compuesto deseado.

Procedimiento general M:

Sustitución de dinitroimidazol

Se agitó una solución de (1 eq.) de 1,4-dinitro-1H-imidazol (documento WO 99/08699) y la amina apropiada (1 - 2 equiv.) en Metanol - agua 1:1 a temperatura ambiente durante 48 horas. El disolvente se retiró a vacío. El residuo se recogió en cloruro de metileno y se cromatografió sobre gel de sílice proporcionando el compuesto deseado.

Procedimiento general N:

Formación de mesilato (A)

Se disolvió el alcohol apropiado (1 equiv.) en piridina y se trató con cloruro de metanosulfonilo (2,2 equiv.) a 0°C. La reacción se calentó hasta T A y se agitó durante 4 horas, se inactivó con bicarbonato sódico, y se extrajo con cloruro de metileno. Se secaron los extractos y se concentraron proporcionando el mesilato apropiado que se usó sin purificación adicional.

Formación de mesilato B

El alcohol apropiado (1 equiv), cloruro de metanosulfonilo (1 equiv), trietilamina (1 equiv) en cloruro de metileno se agitó a T A durante 1 a 8 horas. La mezcla de reacción se inactivó con agua, se separó la fase orgánica y se concentró proporcionando el mesilato deseado que se usó sin purificación adicional.

Procedimiento general O:

Desplazamiento del mesilato

Una solución 0,1 M de mesilato en acetonitrilo se trató con 3 equiv. de

amina y 3 equiv. de K_2CO_3 y se calentó a 65 - 80 °C con agitación durante 24 - 75 horas. Una vez que se juzgó completa mediante APCI o TLC, la reacción se inactivó con H_2O y se extrajo con DCM. La cromatografía de gel de sílice o HPLC produjo el producto puro con un 30 - 75% de rendimiento.

Procedimiento general P:

Desplazamiento por haluro de bencilo

Una solución 0,1 M de imidazol en DMF se trató con 1,1 - 2,1 equiv. de haluro de bencilo y 2,1 equiv. de K_2CO_3 y se calentó a 65 °C con agitación durante 18 - 30 horas. En algunos casos la reacción se facilitó mediante la adición de 0,05 equiv. de Et_3NBnCl. Una vez que se juzgó completa mediante APCI o TLC, la reacción se inactivó con H_2O y se extrajo con EtOAc. Los extractos combinados se lavaron con H_2O y salmuera, se secaron sobre $MgSO_4$, se filtraron y se concentraron. Como alternativa, las reacciones se tratan mediante extracción con DCM. Los extractos se cargaron en un cartucho de SCX SPE (1 g, Siliciclo). Después de lavar con MeOH, se eluyó el producto bruto con TEA 1 N en MeOH. La cromatografía de gel de sílice o HPLC produjo el producto puro con un 30 - 75% de rendimiento.

Procedimiento general R:

Hidrólisis de éster

El éster (1 equiv.) se disuelve en THF:agua (5:1) y se añade LiOH (1,2 equiv.). La reacción se agita durante toda una noche a T A, se retira el disolvente, se añade agua, y el pH se ajusta hasta 7 usando ácido clorhídrico 1 N. Se filtra el sólido, se lava con agua y éter dietílico, y se seca produciendo el ácido deseado.

Los siguientes intermedios se prepararon mediante procedimientos análogos a los descritos anteriormente para el procedimiento general F;

1-(3-metil-oxetan-3-ilmetil)-4-nitro-1H-imidazol; H1 RMN, (CDCl3, 400 MHz) δ 1,25 (s, 3 H), 4,28 (s, 2 H), 4,42 (dd, J = 6,6 Hz, 37,3 Hz, 4 H), 7,44 (s, 1H), 7,80 (s, 1 H).

4-Nitro-1-[1-(4-trifluorometil-fenil)-etil]-1H-imidazol; H1 RMN, (CDCl3, 400 MHz) δ 1,96 (d, 3 H), 5,49 (c, 1 H), 7,33 (d, 2 H), 7,53 (s, 1 H), 7,67 (d, 2 H), 7,78 (s, 1H).

1-Bencil-4-nitro-1H-imidazol; se preparó de acuerdo con el procedimiento de Searcey, M.; Pye, P. L.; Lee, J. B.; Synth. Commun.; EN.; 19; 7,8; 1989; 1309 - 1316.

Éster metílico del ácido 1-(4-nitro-imidazol-1-il)-ciclobutanocarboxílico. EM 240 m/z (M + 1).

Éster metílico del ácido 2-(4-nitro-imidazol-1-il)-ciclobutanocarboxílico. EM 240 m/z (M + 1).

Los siguientes intermedios se prepararon a partir de dinitroimidazol mediante procedimientos análogos a los descritos anteriormente para el procedimiento general M;

1-Indan-1-il-4-nitro-1H-imidazol; EM 230 m/z (M + 1).

(1R, 2S)-(1-(4-nitro-imidazol-1-il)-indan-2-ol; EM 246 m/z (M + 1).

(1S, 2R)-(1-(4-nitro-imidazol-1-il)-indan-2-ol; EM 246 m/z (M + 1).

2-(4-fluorofenil)-2-(4-nitro-1H-imidazol-1-il)-etanol; EM 252 m/z (M + 1).

(2-(4-nitro-1H-imidazol-1-il)-fenil)metanol; EM 220 m/z (M + 1).

2-(4-nitro-1H-imidazol-1-il)-2-fenilacetato de metilo; EM 262 m/z (M + 1).

Los siguientes nitroimidazoles se prepararon mediante procedimientos

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análogos a los descritos anteriormente para el procedimiento general H:

2,2-dimetil-N-(2-(4-nitro-1H-imidazol-1-il)-2-feniletil)propan-1-amina

2-(4-nitro-1H-imidazol-1-il)-2-fenilacetato de metilo se convirtió en el compuesto del título usando un procedimiento análogo al procedimiento general H produciendo el compuesto del título.: EM 303 m/z (M + 1).

Lo siguiente se preparó como sigue:

4-Nitro-1-(2-pirrolidin-1-ilmetil-ciclobutil)-1H-imidazol

Una mezcla del éster metílico del ácido 2-(4-nitro-imidazol-1-il)-ciclobutanocarboxílico (2,640 g, 0,01105 mol), complejo borano-sulfuro de dimetilo (1 M en tetrahidrofurano) (33,2 ml, 0,0332 mol) y tetrahidrofurano (10 ml) se calentó a reflujo durante 17 horas. La reacción se inactivó con agua. El disolvente volátil se evaporó a presión reducida. El residuo se diluyó con agua y se extrajo con acetato de etilo tres veces. Se lavaron los extractos combinados con salmuera y se secaron sobre sulfato de sodio. Después el disolvente se evaporó a presión reducida produciendo [2-(4-nitro-imidazol-1-il)-ciclobutil]-metanol (0,825 g, 0,00419 mol) en forma de un sólido de color blanco. M + 1 = 198,1.

Se convirtió [2-(4-nitro-imidazol-1-il)-ciclobutil]-metanol en el éster 2-(4-nitro-imidazol-1-il)-ciclobutilmetílico del ácido metanosulfónico siguiendo el procedimiento general N; EM 276,3 m/z (M + 1).

Se convirtió el éster 2-(4-nitro-imidazol-1-il)-ciclobutilmetílico del ácido metanosulfónico en el compuesto del título siguiendo el procedimiento general O; EM 251,5 m/z (M + 1).

Los siguientes mesilatos se prepararon mediante procedimientos análogos a los descritos anteriormente para el procedimiento general N:

Éster 2-(4-{2-[2-(3,5-difluorofenil)acetilamino]-pentanoilamino}-imidazol-1-il)-etílico del ácido metanosulfónico

Se convirtió la [1-(2-hidroxietil)-1H-imidazol-4-il]-amida del ácido 2-[2-(3,5-difluorofenil)acetilamino]-pentanoico (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) en el compuesto del título; EM 459,0 m/z (M + 1).

Éster 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino) pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico

Se convirtió la [1-(3-hidroxipropil)-1H-imidazol-4-il]-amida del ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico en el compuesto del título; EM 485 m/z (M + 1).

Éster 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino) pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico

Se convirtió la [1-(2-hidroxi-1-metil-etil)-1H-imidazol-4-il]-amida del ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico en el compuesto del título; EM 485,5 m/z (M + 1).

Éster 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino) pentanoilamino]-imidazol-1-il}-3-metil-butílico del ácido metanosulfónico

Se convirtió la [1-(3-hidroxi-1,1-dimetil-propil)-1H-imidazol-4-il]-amida del ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico en el compuesto del título; EM 513 m/z (M + 1).

Los siguientes intermedios se prepararon mediante procedimientos análogos a los descritos anteriormente para la reducción del nitroimidazol apropiado usando el procedimiento general G seguido del acoplamiento con el ácido apropiado usando el procedimiento general A, procedimiento F.

(1-bencil-1H-imidazol-4-il)-amida del ácido 2-[2-(3,5-difluoro-fenil)-acetilamino]-pentanoico.

Se redujo 1-bencil-4-nitro-1H-imidazol y se acopló con ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico produciendo el compuesto del título; EM 470 m/z (M + 1).

Éster metílico del ácido (4-{2-[2-(3,5-difluoro-fenil)-acetilamino]-pentanoilamino}-imidazol-1-il)-acético.

El éster metílico del ácido (4-nitroimidazol-1-il)-acético se redujo y se acopló con ácido 2-[2-(3,5-difluorofenil)-acetilamino]-pentanoico produciendo el compuesto del título; EM 409,1 m/z (M + 1).

Éster metílico del ácido 1-(4-{2-[2-(3,5-difluoro-fenil)-acetilamino]-pentanoilamino}-imidazol-1-il)-ciclobutanocarboxílico.

El éster metílico del ácido 1-(4-nitro-imidazol-1-il)-ciclobutanocarboxílico se redujo y se acopló con ácido 2-[2-(3,5-difluorofenil)-acetilamino]-pentanoico produciendo el compuesto del título; EM 463,0 m/z (M + 1).

Éster metílico del ácido 2-(4-{2-[2-(3,5-difluoro-fenil)-acetilamino]-pentanoilamino}-imidazol-1-il)-ciclobutanocarboxílico.

El éster metílico del ácido 2-(4-nitro-imidazol-1-il)-ciclobutanocarboxílico se redujo y se acopló con ácido 2-[2-(3,5-difluorofenil)-acetilamino]-pentanoico produciendo el compuesto del título; EM 463,1 m/z (M + 1).

Éster metílico del ácido 1-{4-[2-(5,7-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-ciclobutanocarboxílico.

El éster metílico del ácido 1-(4-nitro-imidazol-1-il)-ciclobutanocarboxílico se redujo y se acopló con ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico produciendo el compuesto del título; EM 475,5 m/z (M + 1).

Éster metílico del ácido 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-propionilamino]-imidazol-1-il}-2-metilpropiónico.

El éster metílico del ácido 2-metil-2-(4-nitro-imidazol-1-il)-propiónico se redujo y se acopló con ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propiónico produciendo el compuesto del título; EM 421,5 m/z (M + 1).

Éster metílico del ácido 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-propiónico.

El éster metílico del ácido 2-(4-nitro-imidazol-1-il)- propiónico se redujo y se acopló con ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico produciendo el compuesto del título; EM 435,5 m/z (M + 1).

Éster metílico del ácido 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-3-metil-butírico.

El éster metílico del ácido 3-metil-3-(4-nitro-imidazol-1-il)-butírico se redujo y se acopló con ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico produciendo el compuesto del título; EM 463,5 m/z (M + 1).

Éster metílico del ácido 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-2-metil-propiónico.

El éster metílico del ácido 2-metil-2-(4-nitro-imidazol-1-il)-propiónico se redujo y se acopló con ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico produciendo el compuesto del título; EM 449,3 m/z (M + 1).

Éster terc-butílico del ácido {1-[1-(3-oxo-butil)-1H-imidazol-4-ilcarbamoil]-butil}carbámico

4-(4-Nitro-1H-imidazol-1-il)-butan-2-ona se redujo y se acopló con ácido 2-[(terc-butoxicarbonil)amino]pentanoico produciendo el compuesto del título; EM 353 m/z (M + 1).

Éster metílico del ácido 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}propiónico; EM 435 m/z (M + 1).

[1-(1-metil-3-oxo-butil)-1H-imidazol-4-il]-amida del ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico; EM 433 m/z (M + 1).

Los siguientes grupos Boc se retiraron siguiendo el procedimiento general D;

Clorhidrato de la [1-(3-oxo-butil)-1H-imidazol-4-il]-amida del ácido 2-amino-pentanoico; EM 253 m/z (M + 1).

{1-[2-(2,6-dimetil-morfolin-4-il)-1,1-dimetil-etil]-1H-imidazol-4-il}-amida del ácido 2- amino-pentanoico; EM 352,3 m/z (M + 1).

(1-{1,1-dimetil-3-[(piridin-2-ilmetil)-amino]-propil}-1H-imidazol-4-il)-amida del ácido 2- amino-pentanoico; EM 359 m/z (M + 1).

{1-[1,1-dimetil-3-(2,2,2-trifluoro-1-fenil-etilamino)-propil]-1H-imidazol-4-il}-amida del ácido 2- amino-pentanoico; EM 426 m/z (M + 1).

{1-[1,1-dimetil-3-(1-fenil-etilamino)propil]-1H-imidazol-4-il}-amida del ácido 2- amino-pentanoico; EM 372 m/z (M + 1).

Los siguientes alcoholes se prepararon mediante reducción de los ésteres correspondientes usando los procedimientos análogos a los descritos anteriormente usando el procedimiento general I;

[1-(2-hidroxi-etil)-1H-imidazol-4-il]-amida del ácido 2-[2-(3,5-difluoro-fenil)-acetilamino]-pentanoico; EM 381,1 m/z (M + 1).

[1-(3-hidroxipropil)-1H-imidazol-4-il]-amida del ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)pentanoico; EM 407 m/z (M + 1).

[1-(2-hidroxi-1-metil-etil)-1H-imidazol-4-il]-amida del ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)pentanoico; EM 407,5 m/z (M + 1).

Éster terc-butílico del ácido {1-[1-(3-hidroxi-1,1-dimetil-propil)-1H-imidazol-4-ilcarbamoil]-butil}-carbámico; EM 369 m/z (M + 1).

Los siguientes aldehídos se prepararon mediante oxidación a partir del alcohol correspondiente usando los procedimientos análogos a los descritos anteriormente usando el procedimiento general J;

[1-(1-formil-ciclobutil)-1H-imidazol-4-il]amida del ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico; EM 419,1 m/z (M + 1).

[1-(1-formil-ciclobutil)-1H-imidazol-4-il]amida del ácido 2-(5,7-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico; EM 431,5 m/z (M + 1).

(2S)-2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-3-ilamino)-N-(1-(2-formilfenil)-1H-imidazol-4-il)pentanamida;

Éster terc-butílico del ácido {1-[1-(1,1-dimetil-3-oxo-propil)-1H-imidazol-4-ilcarbamoil]-butil}-carbámico; EM 367 m/z (M + 1).

Los siguientes ácidos se prepararon mediante hidrólisis de lso ésteres correspondientes usando procedimientos análogos a lso descritos anteriormente usando el procedimiento general R;

Éster metílico del ácido 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)pentanoilamino]-imidazol-1-il}-3-metil-butírico; EM 449,6 m/z (M + 1).

Ácido 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino) pentanoilamino]-imidazol-1-il}-2-metil-propiónico; EM 435,4 m/z (M + 1).

Ácido 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino) propionilamino]-imidazol-1-il}-2-metil-propiónico; EM 407,5 m/z (M + 1).

Procedimiento para la síntesis de ácido 2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico, procedimiento general Q:

Combinar el clorhidrato del éster metílico de L-norvalina (1 equiv.) con

6,8-difluoro-3,4-dihidro-1H-naftalen-2-ona (1 equiv.) en cloruro de metileno y agitar 30 min, y añadir triacetoxi borohidruro de sodio (1,1 equiv.) y agitar a T A durante toda una noche. La reacción se inactiva con bicarbonato sódico acuoso, se extrae con cloruro de metileno, se seca y se concentra. El material resultante se purifica mediante cromatografía en gel de sílice produciendo los diastereómeros separados del éster metílico del ácido 2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen- 2-ilamino)-pentanoico. Diastereómero 1; ^{13}C RMN ($CDCl_3$, 100 MHz) 14,0, 19,4, 27,7, 28,2, 29,5, 29,6, 36,3, 51,1, 58,7, 100,7, 100,9, 101,2, 110,5, 110,7, 110,8, 118,5, 118,6, 141,1, 159,7, 159,8, 162,1, 176,7; EM m/z 298,3 (M + 1). Diastereómero 2; Diagnóstico 13C RMN ($CDCl_3$, 100 MHz) 14,0, 19,3, 28,3, 28,4, 28,5, 30,3, 36,4, 51,1, 52,0, 58,5, 100,7, 100,9, 101,2, 110,5, 110,7, 176,8; EM m/z 298,3 (M + 1).

Se disuelve el éster metílico del ácido 2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico (1 equiv.) en THF: agua (5:1) y se añade LiOH (1,2 equiv.) La reacción se agita durante toda una noche a T A, el disolviente se retira, se añade agua, y el pH se ajusta hasta 7 usando ácido clorhídrico 1 N. Se filtra el sólido, se lavó con agua y éter dietílico, y se seca produciendo ácido 2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen- 2-ilamino)-pentanoico. Ácido derivado del diastereómero 1; H1 RMN (CD3OD, 400 MHz) 0,99 (t, 3H, J = 7,5), 1,48 (m, 2H), 1,82 (m, 3H), 2,36 (m, 1H), 2,65 (m, 1H), 2,95 (m, 2H), 3,28 (s, 1H), 3,42 (m, 1H), 3,74 (m, 1H), 6,80 (m, 2H); (EM m/z 284,3 (M + 1). Ácido derivado del diastereómero 2: H1 RMN (CD3OD, 400 MHz) 0,94 (t, 3H, J = 7,6), 1,42 (m, 2H), 1,56 (m, 3H), 1,96 (m, 1H), 2,25 (m, 1H), 2,85 (m, 3H), 3,15 (m, 1H), 3,25 (m, 1H), 6,64 (m, 2H); EM m/z 284,2 (M + 1).

Los siguientes intermedios se prepararon de una manera análoga al

procedimiento Q partiendo de un aminoácido y cetona apropiados o amino-éster y cetona de partida; o el aminoéster se acila usando el procedimiento general A seguido de hidrólisis.

Ácido (S)-2-(2-(3,5-difluorofenil)acetamido)-2-fenilacético; EM 304 m/z (M - 1).

Ácido (S)-2-(2-(3,5-difluorofenil)acetamido)-2-(piridin-3-il)-acético; EM 305 m/z (M - 1).

Ácido (S)-2-(2-(3,5-difluorofenil)acetamido)-2-(4-fluorofenil)acético; EM 322 m/z (M - 1).

Ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-3-ilamino)-2-fenilacético; EM 316 m/z (M - 1).

Ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propiónico; EM 256,5 m/z (M + 1).

Ácido (S)-2-(1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico; EM 246,5 m/z (M - 1).

Los siguientes intermedios se prepararon de una manera análoga al procedimiento B partiendo de una amina apropiada y cetona/aldehído.

Éster terc-butílico del ácido (1-{1-[2-(2,6-dimetil-morfolin-4-il)-1,1-dimetil-etil]-1H-imidazol-4-ilcarbamoil}-butil)-carbámico; EM 452,1 m/z (M + 1).

[1-(3-oxobutil)-1H-imidazol-4-il]amida del ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico; EM 419 m/z (M + 1).

Éster terc-butílico del ácido [1-(1-{1,1-dimetil-3-[(piridin-2-ilmetil)amino]-propil}-1H-imidazol-4-ilcarbamoil)-butil]-carbámico; EM 459 m/z (M + 1).

Éster terc-butílico del ácido (1-{1-[1,1-dimetil-3-(2,2,2-trifluoro-1- fenil-etilamino)-propil]-1H-imidazol-4-ilcarbamoil-butil)-carbámico; EM 526 m/z (M +

1).

Éster terc-butílico del ácido (1-{1-[1,1-dimetil-3-(1- fenil-etilamino)-propil]-1H-imidazol-4-ilcarbamoil}-butil)-carbámico; EM 472 m/z (M + 1).

Los siguientes ejemplos se prepararon mediante procedimientos análogos a los descritos anteriormente para el procedimiento general O;

Ejemplo 1

{1-[2-(3-etoxi-propilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con 3-etoxipropil amina proporcionando el compuesto del título: EM 446,2 m/z (M + 1).

Ejemplo 2

{1-[2-(octahidro-pirazino[1,2-a]azepin-2-il)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 517,2 m/z (M + 1).

Ejemplo 3

{1-[2-([1,4]-dioxan-2-ilmetil-metilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 494,2 m/z (M + 1).

Ejemplo 4

{1-[2-(2-metoxi-1-metil-etilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 452,2 m/z (M + 1).

Ejemplo 5

{1-[2-(3-oxo-piperazin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 463,2 m/z (M + 1).

Ejemplo 6

[1-(2-bencilamino-etil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 470,2 m/z (M + 1).

Ejemplo 7

{1-[2-(3-butoxi-propilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-

pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 494,2 m/z (M + 1).

Ejemplo 8

{1-[2-((1R,2S)-2-hidroximetil-ciclohexilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 492,2 m/z (M + 1).

Ejemplo 9

{1-[(4aS, 8aS)-2-(octahidro-isoquinolin-2-il)etil]-1H-imidazol-4-il}amida del ácido 2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 502,2 m/z (M + 1).

Ejemplo 10

{1-[2-(3-isopropoxi-propilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 480,2 m/z (M + 1).

Ejemplo 11

{1-[2-(octahidro-isoquinolin-2-il)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-

(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 502,2 m/z (M + 1).

Ejemplo 12

{1-[2-(3,4,5,6-tetrahidro-2H-[4,4']bipiridinil-1-il)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 525,2 m/z (M + 1).

Ejemplo 13

{1-[2-(2-hidroxi-2-fenil-etilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 500,2 m/z (M + 1).

Ejemplo 14

{1-[2-(indan-1-ilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 496,2 m/z (M + 1).

Ejemplo 15

{1-[2-(bencil-metilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 484,2 m/z (M + 1).

Ejemplo 16

{1-[2-(indan-2-ilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 496,2 m/z (M + 1).

Ejemplo 17

{1-[2-(3,4-dihidro-1H-isoquinolin-2-il)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 496,2 m/z (M + 1).

Ejemplo 18

{1-[2-(2-propoxi-etilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 466,2 m/z (M + 1).

Ejemplo 19

{1-[2-(3-bencil-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 524,2 m/z (M + 1).

Ejemplo 20

{1-[2-(3-piridin-2-il-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 511,2 m/z (M + 1).

Ejemplo 21

{1-[2-(metil-piridin-4-ilmetil-amino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 485,2 m/z (M + 1).

Ejemplo 22

(1-{2-[(2-metanosulfonil-etil)metil-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2- [2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 500,1 m/z (M + 1).

Ejemplo 23

{1-[2-(2-terc-butoxi-etilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 480,2 m/z (M + 1).

Ejemplo 23A

{1-[2-(3-piridin-4-il-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar el éster 2-(4-{2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoilamino}-imidazol-1-il)etílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 511,2 m/z (M + 1).

Los siguientes ejemplos se prepararon mediante procedimientos análogos a los descritos anteriormente para el procedimiento general P;

Ejemplo 24

[1-(2-fluoro-bencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar la (1H-imidazol-4-il)-amida del ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico con el haluro de bencilo apropiado proporcionando el compuesto del título: EM 445,1 m/z (M + 1).

Ejemplo 25

[1-(3-fluoro-bencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar la (1H-imidazol-4-il)-amida del ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico con el haluro de bencilo apropiado proporcionando el compuesto del título: EM 445,1 m/z (M + 1).

Ejemplo 26

[1-(4-metilbencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar la (1H-imidazol-4-il)-amida del ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico con el haluro de bencilo apropiado proporcionando el compuesto del título: EM 441,1 m/z (M + 1).

Ejemplo 27

[1-(4-metoxibencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar la (1H-imidazol-4-il)-amida del ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico con el haluro de bencilo apropiado proporcionando el compuesto del título: EM 457,3 m/z (M + 1).

Ejemplo 28

[1-(4-terc-butil-bencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar la (1H-imidazol-4-il)-amida del ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico con el haluro de bencilo apropiado proporcionando el compuesto del título: EM 483,3 m/z (M + 1).

Los siguientes ejemplos se prepararon mediante procedimientos análogos a los descritos anteriormente para el procedimiento general B;

Ejemplo 29

[1-(1-pirrolidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar la [1-(1-formil-ciclobutil)-1H-imidazol-4-il]-amida del ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico con la amina apropiada proporcionando el compuesto del título: EM 474,1 m/z (M + 1).

Ejemplo 30

[1-(1-dimetilaminometil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar la [1-(1-formil-ciclobutil)-1H-imidazol-4-il]-amida del ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico con la amina apropiada proporcionando el compuesto del título: EM 448,5 m/z (M + 1).

Ejemplo 31

[1-(1-piperidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-

difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar la [1-(1-formil-ciclobutil)-1H-imidazol-4-il]-amida del ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico con la amina apropiada proporcionando el compuesto del título: EM 488,5 m/z (M + 1).

Ejemplo 32

[1-(1-morfolin-4-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar la [1-(1-formil-ciclobutil)-1H-imidazol-4-il]-amida del ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico con la amina apropiada proporcionando el compuesto del título: EM 490,5 m/z (M + 1).

Ejemplo 31A

(1-{1-[((2R, 6S)-2,6-dimetil-morfolin-4-il)metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar la [1-(1-formil-ciclobutil)-1H-imidazol-4-il]-amida del ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico con la amina apropiada proporcionando el compuesto del título: EM 518,5 m/z (M + 1).

Ejemplo 32A

(1-{1-[(2,2,2-trifluoro-etilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar la [1-(1-formil-ciclobutil)-1H-imidazol-4-il]-amida del ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico con la amina apropiada proporcionando el compuesto del título: EM 502,4 m/z (M + 1).

Ejemplo 33

(1-{1-[((R)-1-ciclohexil-etilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar la [1-(1-formil-ciclobutil)-1H-imidazol-4-il]-amida del ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico con la amina apropiada proporcionando el compuesto del título: EM 530,5 m/z (M + 1).

Ejemplo 34

[1-(1-pirrolidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se hizo reaccionar la [1-(1-formil-ciclobutil)-1H-imidazol-4-il]-amida del ácido 2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico con la amina apropiada proporcionando el compuesto del título: EM 486,5 m/z (M + 1).

Ejemplo 35

(1-{1-[(2,2-dimetil-propilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico

Se hizo reaccionar la [1-(1-formil-ciclobutil)-1H-imidazol-4-il]-amida del ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico con la amina apropiada proporcionando el compuesto del título: EM 490,5 m/z (M + 1).

Ejemplo 36

(1-{1-[(2,2,2-trifluoroetilamino)metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se hizo reaccionar la [1-(1-formil-ciclobutil)-1H-imidazol-4-il]-amida del ácido 2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico con la amina apropiada proporcionando el compuesto del título: EM 514,5 m/z (M + 1).

Ejemplo 37

(1-{1-[(2,2-dimetil-propilamino)metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se hizo reaccionar la [1-(1-formil-ciclobutil)-1H-imidazol-4-il]-amida del ácido 2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico con la amina apropiada proporcionando el compuesto del título: EM 502,6 m/z (M + 1).

Ejemplo 38

(1-{1-[((R)-1-ciclohexil-etilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico

Se hizo reaccionar la [1-(1-formil-ciclobutil)-1H-imidazol-4-il]-amida del ácido 2-(5,7-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico con la amina apropiada proporcionando el compuesto del título: EM 542,6 m/z (M + 1).

Ejemplo 39

[1-(1-dimetilaminometil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico

Se hizo reaccionar la [1-(1-formil-ciclobutil)-1H-imidazol-4-il]-amida del ácido 2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico con la amina apropiada proporcionando el compuesto del título: EM 460,6 m/z (M + 1).

Ejemplo 40

[1-(1-piperidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico

Se hizo reaccionar la [1-(1-formil-ciclobutil)-1H-imidazol-4-il]-amida del ácido 2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico con la amina apropiada proporcionando el compuesto del título: EM 500,6 m/z (M + 1).

Ejemplo 41

[1-(1-morfolin-4-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico

Se hizo reaccionar la [1-(1-formil-ciclobutil)-1H-imidazol-4-il]-amida del ácido 2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico con la amina apropiada proporcionando el compuesto del título: EM 502,6 m/z (M + 1).

Ejemplo 42

(1-{1-[((2R, 6S)-2,6-dimetil-morfolin-4-il)metil]ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico

Se hizo reaccionar la [1-(1-formil-ciclobutil)-1H-imidazol-4-il]-amida del

ácido 2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico con la amina apropiada proporcionando el compuesto del título: EM 530,6 m/z (M + 1).

Ejemplo 43

{1-[2-((R)-1-ciclohexil-etilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico

Se trató la [1-(1,1-dimetil-2-oxo-etil)-1H-imidazol-4-il]-amida del ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico (documento U.S. N° de serie 11/078.898 presentado el 11 de marzo de 2005) con la amina apropiada proporcionando el compuesto del título: EM 530,4 m/z (M + 1).

Ejemplo 44

(1-{1,1-dimetil-2-[(tetrahidropiran-4-ilmetil)amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico

Se trató la [1-(1,1-dimetil-2-oxo-etil)-1H-imidazol-4-il]-amida del ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico (documento U.S. N° de serie 11/078.898 presentado el 11 de marzo de 2005) con la amina apropiada proporcionando el compuesto del título: EM 518,4 m/z (M + 1).

Ejemplo 45

(1-{2-[(1-hidroxi-ciclohexilmetil)-amino]-1,1-dimetil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico

Se trató la [1-(1,1-dimetil-2-oxo-etil)-1H-imidazol-4-il]-amida del ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico (documento U.S.

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Nº de serie 11/078.898 presentado el 11 de marzo de 2005) con la amina apropiada proporcionando el compuesto del título: EM 532,6 m/z (M + 1).

Ejemplo 46

(1-{2-[(4-hidroxi-tetrahidro-piran-4-ilmetil)-amino]-1,1-dimetil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico

Se trató la [1-(1,1-dimetil-2-oxo-etil)-1H-imidazol-4-il]-amida del ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico (documento U.S. Nº de serie 11/078.898 presentado el 11 de marzo de 2005) con la amina apropiada proporcionando el compuesto del título: EM 534,6 m/z (M + 1).

Ejemplo 47

{1-[2-(2-metoxi-2-metilpropilamino)-1,1-dimetil-etil]-1H-imidazol- 4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)- pentanoico

Se trató la [1-(1,1-dimetil-2-oxo-etil)-1H-imidazol-4-il]-amida del ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico (documento U.S. Nº de serie 11/078.898 presentado el 11 de marzo de 2005) con la amina apropiada proporcionando el compuesto del título: EM 506,5 m/z (M + 1).

Ejemplo 48

(1- {1,1-dimetil-2-[(3-metiloxetan-3-ilmetil)-amino]etil}-1H-imidazol- 4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)- pentanoico

Se trató la [1-(1,1-dimetil-2-oxo-etil)-1H-imidazol-4-il]-amida del ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico (documento U.S.

Nº de serie 11/078.898 presentado el 11 de marzo de 2005) con la amina apropiada proporcionando el compuesto del título: EM 504,5 m/z (M + 1).

Ejemplo 49

{1-[2-(ciclohexilmetil-amino)-1,1-dimetil-etil]-1H-imidazol- 4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)- pentanoico

Se trató la [1-(1,1-dimetil-2-oxo-etil)-1H-imidazol-4-il]-amida del ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico (documento U.S. Nº de serie 11/078.898 presentado el 11 de marzo de 2005) con la amina apropiada proporcionando el compuesto del título: EM 516,6 m/z (M + 1).

Ejemplo 50

{1-[2- ((R)-1-ciclohexiletil-amino)-1,1-dimetil-etil]-1H-imidazol- 4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]- pentanoico

Se trató la [1-(1,1-dimetil-2-oxo-etil)-1H-imidazol-4-il]-amida del ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico (documento U.S. Nº de serie 11/078.898 presentado el 11 de marzo de 2005) con la amina apropiada proporcionando el compuesto del título: EM 518,2 m/z (M + 1).

Ejemplo 51

(1-{1,1-dimetil-2-[(tetrahidro-piran-4-ilmetil)-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se trató la [1-(1,1-dimetil-2-oxo-etil)-1H-imidazol-4-il]-amida del ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico (documento U.S. Nº de serie 11/078.898 presentado el 11 de marzo de 2005) con la amina apropiada

proporcionando el compuesto del título: EM 506,4 m/z (M + 1).

Ejemplo 52

{1-[3-((S)-1-fenil-etilamino)-butil]-1H-imidazol- 4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico

Se trató la [1-(3-oxo-butil)-1H-imidazol-4-il]-amida del ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico con la amina apropiada proporcionando el compuesto del título: EM 524,1 m/z (M + 1).

Ejemplo 53

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1-H-imidazol-4-il]amida del ácido (S)-2-(diciclopropilmetil-amino)-pentanoico

Se trató la [1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido 2-amino-pentanoico (documento U.S. Nº de serie 11/078.898 presentado el 11 de marzo de 2005) con la cetona apropiada proporcionando el compuesto del título: EM 402,6 m/z (M + 1).

Los siguientes ejemplos se prepararon mediante procedimientos análogos a los descritos anteriormente para el procedimiento general I;

Ejemplo 54

[1-(1-hidroximetil-ciclobutil)-1-H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se redujo el éster metílico del ácido 1-(4-{2-[2-(3,5-difluoro-fenil) acetilamino]pentanoilamino}-imidazol-1-il)-ciclobutanocarboxílico proporcionando el compuesto del título: EM 421,1 m/z (M + 1).

Ejemplo 55

[1-(2-hidroximetil-ciclobutil)-1-H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico

Se redujo el éster metílico del ácido 2-(4-{2-[2-(3,5-difluoro-fenil) acetilamino]pentanoilamino}-imidazol-1-il)-ciclobutanocarboxílico proporcionando el compuesto del título: EM 421,1 m/z (M + 1).

Ejemplo 56

[1-(1-hidroximetil-ciclobutil)-1-H-imidazol-4-il]amida del ácido (S)-2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se redujo el éster metílico del ácido 1-{4-[2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)pentanoilamino]-imidazol-1-il}-ciclobutanocarboxílico proporcionando el compuesto del título: EM 433,5 m/z (M + 1).

Los siguientes ejemplos se prepararon mediante procedimientos análogos a los descritos anteriormente para el procedimiento general K;

Ejemplo 57

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(2,4- difluoro-fenil)-2-hidroxietilamino]-pentanoico

Se trató la [1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido 2-amino-pentanoico (documento U.S. Nº de serie 11/078.898 presentado el 11 de marzo de 2005) con el epóxido apropiado proporcionando el compuesto del título: EM 464,3 m/z (M + 1).

Ejemplo 58

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,4- difluoro-fenil)-2-hidroxietilamino]-pentanoico

Se trató la [1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido 2-amino-pentanoico (documento U.S. Nº de serie 11/078.898 presentado el 11 de marzo de 2005) con el epóxido apropiado proporcionando el compuesto del título: EM 464,3 m/z (M + 1).

Ejemplo 59

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)-2-hidroxietilamino]-pentanoico

Se trató la [1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido 2-amino-pentanoico (documento U.S. Nº de serie 11/078.898 presentado el 11 de marzo de 2005) con el epóxido apropiado proporcionando el compuesto del título: EM 464,5 m/z (M + 1).

Ejemplo 60

{1-[2-((2R, 6S)-2,6-dimetil-morfolin-4-il)-1,1-dimetil-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-[2- (2,4-difluoro-fenil)-2-hidroxietilamino]-pentanoico

Se trató la [1-(1,1-dimetil-2-(2,6-dimetilmorfolino-1-il-etil)-1H-imidazol-4-il]-amida del ácido 2-amino-pentanoico con el epóxido apropiado proporcionando el compuesto del título: EM 508,5 m/z (M + 1).

Ejemplo 61

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido (S)-2-[(1-hidroxiciclohexilmetil)amino]-pentanoico

Se trató la [1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido 2-amino-pentanoico (documento U.S. Nº de serie 11/078.898 presentado el 11 de marzo de 2005) con el epóxido apropiado proporcionando el compuesto del título: EM 420,6 m/z (M + 1).

Los siguientes ejemplos se prepararon mediante procedimientos análogos a los descritos anteriormente para el procedimiento general O;

Ejemplo 62

{1-[3-((R)-1-fenil-etilamino)propil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se trató el éster 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 510,1 m/z (M + 1).

Ejemplo 63

{1-[3-(3-metil-bencilamino)-propil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se trató el éster 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 510,53 m/z (M + 1).

Ejemplo 64

{1-[3-(2-hidroxi-2-fenil-etilamino)-propil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se trató el éster 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 526,54 m/z (M + 1).

Ejemplo 65

{1-[3-(2-cloro-bencilamino)-propil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se trató el éster 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 530,5 m/z (M + 1).

Ejemplo 66

{1-[3-(3,4-dihidro-1H-isoquinolin-2-il)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se trató el éster 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 522,53 m/z (M + 1).

Ejemplo 67

{1-[3-(indan-2-ilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se trató el éster 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 522,52 m/z (M + 1).

Ejemplo 68

{1-[3-(1-metoximetil-propilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se trató el éster 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 492,53 m/z (M + 1).

Ejemplo 69

{1-[3-(4-cloro-bencilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se trató el éster 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 530,5 m/z (M + 1).

Ejemplo 70

{1-[3-(2-metilbencilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-

difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se trató el éster 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 510,5 m/z (M + 1).

Ejemplo 71

{1-[3-(2-metoxietilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se trató el éster 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 464,2 m/z (M + 1).

Ejemplo 72

(1-{3-[(piridin-3-ilmetil)amino]-propil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se trató el éster 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 497,5 m/z (M + 1).

Ejemplo 73

{1-[3-((S)-1-p-tolil-etilamino)propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se trató el éster 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 524,6 m/z (M + 1).

Ejemplo 74

{1-[3-(4-metoxibencilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se trató el éster 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 526,5 m/z (M + 1).

Ejemplo 75

{1-[3-(ciclopropilmetilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se trató el éster 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 460,5 m/z (M + 1).

Ejemplo 76

{1-[3-(4-metilbencilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se trató el éster 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-

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ilamino)-pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico con la amina apropiada proporcionando el compuesto del título: EM 510,5 m/z (M + 1).

Los siguientes ejemplos se prepararon mediante procedimientos análogos a los descritos anteriormente para el procedimiento general A, procedimiento F usando el ácido 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-2-metil-propiónico y una amina apropiada.

Ejemplo 77

{1-[1-metil-1-(metilfenetil-carbamoil)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

EM 552,58 m/z (M + 1).

Ejemplo 78

{1-[1-(1,3-dihidro-isobenzofuran-5-ilcarbamoil)-1-metil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

EM 552,55 m/z (M + 1).

Ejemplo 79

{1-[1-(indan-1-ilcarbamoil)-1-metil-etil]-1H-imidazol-4- il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

EM 550,53 m/z (M + 1).

Ejemplo 80

{1-[1,1-dimetil-2-oxo-2-(3-piridin-4-il-pirrolidin-1-il)-etil]-1H-imidazol-4- il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico

EM 565,6 m/z (M + 1).

Ejemplo 81

(1-{1-[2-(3-fluoro-fenil)-etilcarbamoil]-1-metiletil}-1H-imidazol-4- il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

EM 556,54 m/z (M + 1).

Ejemplo 82

{1-[2-(3-ciano-piperidin-1-il)-1,1-dimetil-2-oxo-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

EM 527,57 m/z (M + 1).

Ejemplo 83

(1-{1-metil-1-[metil-(tetrahidro-piran-2-ilmetil)carbamoil]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

EM 546,58 m/z (M + 1).

Ejemplo 84

(1-{1-[etil-(2-pirazol-1-il-etil)carbamoil]-1-metiletil}-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

EM 556,61 m/z (M + 1).

Ejemplo 85

{1-[1,1-dimetil-2-oxo-2-(2-fenil-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

EM 564,59 m/z (M + 1).

Ejemplo 86

(1-{1-[(furan-2-ilmetil)carbamoil]-1-metiletil}-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

EM 514,51 m/z (M + 1).

Ejemplo 87

(1-{2-[3-(acetil-metil-amino)pirrolidin-1-il]-1,1-dimetil-2-oxo-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

EM 559,57 m/z (M + 1).

Ejemplo 88

{1-[1-metil-1-((3R, 4S)-4-metilsulfanil-tetrahidro-furan-3-ilcarbamoil)etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

EM 550,53 m/z (M + 1).

Ejemplo 89

{1-[2-(4-acetil-[1,4]diazepan-1-il)-1,1-dimetil-2-oxo-etil]-1H- imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

EM 559,31 m/z (M + 1).

Ejemplo 90

(1-{1-metil-1-[1-(1-metil-1H-pirazol-4-il)etilcarbamoil]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

EM 542,56 m/z (M + 1).

Ejemplo 91

{1-[1-(3-metoxi-propilcarbamoil)-1-metiletil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

EM 506,52 m/z (M + 1).

Ejemplo 92

(1-{1-metil-1-[(3-metil-[1,2,4]oxadiazol-5-ilmetil)carbamoil]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

EM 530,54 m/z (M + 1).

Ejemplo 93

(1-{1-[(2-ciano-etil)-metilcarbamoil]-1-metil-etil}-1H-imidazol-4- il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

EM 501,51 m/z (M + 1).

Ejemplo 94

{1-[1,1-dimetil-2-(3-metil-5,6-dihidro-8H-[1,2,4]triazolo[4,3-a]pirazin-7-il)-2-oxo-

etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico

EM 555,55 m/z (M + 1).

Ejemplo 95

(1-{1-metil-1-[metil-(1-metil-1H-imidazol-2-ilmetil)carbamoil]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

EM 542,48 m/z (M + 1).

Ejemplo 96

(1-{1-[(2-dietilamino-etil)metil-carbamoil]-1-metil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

EM 547,62 m/z (M + 1).

Los siguientes ejemplos se prepararon mediante procedimientos análogos a los descritos anteriormente para el procedimiento general A, procedimiento F usando el ácido 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-2-metil-propiónico y una amina apropiada.

Ejemplo 97

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)propionilamino]-imidazol-1-il}-N-indan-1-il-isobutiramida

EM 522,56 m/z (M + 1).

Ejemplo 98

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino) -N-{1- [1,1-dimetil-2-oxo-2-(3-piridin-4-il-pirrolidin-1-il)etil]-1H-imidazol-4-il}- propionamida

EM 537,53 m/z (M + 1).

Ejemplo 99

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino) -N-{1- [2-(4-hidroximetil-4-metilpiperidin-1-il)-1,1-dimetil-2-oxo-etil]-1H-imidazol-4-il} propionamida

EM 528,51 m/z (M + 1).

Ejemplo 100

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)propionilamino]-imidazol-1-il}-N-metil-N-fenetil-isobutiramida

EM 524,54 m/z (M + 1).

Ejemplo 101

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)propionilamino]-imidazol-1-il}-N-etil-N-(2-pirazol-1-il-etil)-isobutiramida

EM 528,49 m/z (M + 1).

Ejemplo 102

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1-[2-(4- hidroximetil-4-metil-piperidin-1-il)-1,1-dimetil-2-oxo-etil]-1H-imidazol-4-il}- propionamida

EM 518,53 m/z (M + 1).

Ejemplo 103

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-(4-metilbencil)-isobutiramida

EM 510,49 m/z (M + 1).

Ejemplo 104

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-(1,3-dihidro-isobenzofuran-5-il)-isobutiramida

EM 524,47 m/z (M + 1).

Ejemplo 105

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1-[1,1-dimetil-2-oxo-2-(2-fenilpirrolidin-1-il)-etil]-1H-imidazol-4-il}-propionamida

EM 536,55 m/z (M + 1).

Ejemplo 106

(S)-N-{1-[2-(3-ciano-piperidin-1-il)-1,1-dimetil-2-oxo-etil]-1H-imidazol-4-il}-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionamida

EM 499,46 m/z (M + 1).

Ejemplo 107

(S)-N-(1-{2-[3-(acetil-metil-amino)-pirrolidin-1-il]-1,1-dimetil-2-oxo-etil}-1H-imidazol-4-il)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionamida

EM 531,53 m/z (M + 1).

Ejemplo 108

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-((1R, 2S)-2-hidroximetil-ciclohexil)isobutiramida

EM 518,53 m/z (M + 1).

Ejemplo 109

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-(3-metil-[1,2,4]oxadiazol-5-ilmetil)isobutiramida

EM 502,43 m/z (M + 1).

Ejemplo 110

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-((S)-2-metoxi-1-metil-etil)isobutiramida

EM 478,51 m/z (M + 1).

Ejemplo 111

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-(3-metoxipropil)isobutiramida

EM 478,58 m/z (M + 1).

Ejemplo 112

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-[1-(1-metil-1H-pirazol-4-il)-etil]-isobutiramida

EM 514,51 m/z (M + 1).

Ejemplo 113

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-(3-imidazol-1-il-propil)-isobutiramida

EM 514,56 m/z (M + 1).

Ejemplo 114

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-(3-morfolin-4-il-propil)-isobutiramida

EM 533,58 m/z (M + 1).

Los siguientes ejemplos se prepararon mediante procedimientos análogos a los descritos anteriormente para la reducción del nitroimidazol apropiado usando el procedimiento general G seguido de acoplamiento con el ácido apropiado usando el procedimiento general A, procedimiento F.

Ejemplo 115

[1-(3-metil-oxetan-3-ilmetil)-1H-imidazol-4-il]-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se redujo 1-(3-metiloxetan-3-ilmetil)-4-nitro-1H-imidazol y después se acopló con el ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) produciendo el compuesto del título; EM 433,3 m/z (M + 1).

Ejemplo 116

[1-(3-metil-oxetan-3-ilmetil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-

(3,5- difluoro-fenil)acetilamino]-pentanoico

Se redujo 1-(3-metiloxetan-3-ilmetil)-4-nitro-1H-imidazol y después se acopló con el ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) produciendo el compuesto del título; EM 421,3 m/z (M + 1).

Ejemplo 117

{1-[1-(4-trifluorometilfenil)etil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se redujo 4-nitro-1-[1-(4-trifluorometilfenil)etil]-1H-imidazol y después se acopló con el ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) produciendo el compuesto del título; EM 521,5 m/z (M + 1).

Ejemplo 118

{1-[1-(4-trifluorometil-fenil)-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico

Se redujo 4-nitro-1-[1-(4-trifluorometilfenil)etil]-1H-imidazol y después se acopló con el ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) produciendo el compuesto del título; EM 509,5 m/z (M + 1).

Ejemplo 120

[1-(2-pirrolidin-1-ilmetilciclobutil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico

760

Se redujo 4-nitro-1-(2-pirrolidin-1-ilmetil-ciclobutil)-1H-imidazol y después se acopló con el ácido 2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) produciendo el compuesto del título; EM 474,6 m/z (M + 1).

Ejemplo 121

[1-(2-pirrolidin-1-ilmetilciclobutil)-1H-imidazol-4-il]-amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se redujo 4-nitro-1-(2-pirrolidin-1-ilmetil-ciclobutil)-1H-imidazol y después se acopló con el ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) produciendo el compuesto del título; EM 486,6 m/z (M + 1).

Ejemplo 122

(1-{1,1-dimetil-2-[(tetrahidro-piran-4-ilmetil)-amino]-etil}-1H-imidazol-4-il)-amida del ácido (S)-2- (1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se redujo [2-(4-nitro-imidazol-1-il)propil]-(tetrahidropiran-4-ilmetil)-amina y después se acopló con el ácido 2-(1,2,3,4-tetrahidronaftalen-2- ilamino)-pentanoico produciendo el compuesto del título; EM 482,6 m/z (M + 1).

Ejemplo 123

{1-[2-(2-etoxi-etilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se redujo (2-etoxi-etil)-[2-metil-2-(4-nitroimidazol-1-il)-propil]-amina y después se acopló con el ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-

ilamino)-pentanoico (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) produciendo el compuesto del título; EM 492,6 m/z (M + 1).

Ejemplo 124

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1-[2-(2-etoxi-etilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-propionamida

Se redujo (2-etoxi-etil)-[2-metil-2-(4-nitroimidazol-1-il)-propil]-amina y después se acopló con el ácido 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propiónico produciendo el compuesto del título; EM 464,6 m/z (M + 1).

Los siguientes ejemplos se prepararon mediante procedimientos análogos a los descritos anteriormente para el procedimiento general A, procedimiento F

Ejemplo 125

(1-{2-[(1-hidroxi-ciclohexilmetil)-carbamoil]-1,1-dimetil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se acopló el ácido 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-3-metil-butírico con la amina apropiada produciendo el compuesto del título; EM 560,5 m/z (M + 1).

Ejemplo 126

(1-{1-[(1-hidroxi-ciclohexilmetil)-carbamoil]-1-metil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se acopló el ácido 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-2-metil-propiónico con la amina apropiada produciendo el compuesto del título; EM 546,6 m/z (M + 1).

Ejemplo 127

(1-{1-metil-1-[(tetrahidro-piran-4-ilmetil)-carbamoil]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se acopló el ácido 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-2-metil-propiónico con la amina apropiada produciendo el compuesto del título; EM 532,6 m/z (M + 1).

Ejemplo 128

{1-[1-metil-1-(2-metil-bencilcarbamoil)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se acopló el ácido 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-2-metil-propiónico con la amina apropiada produciendo el compuesto del título; EM 538,52 m/z (M + 1).

Ejemplo 129

{1-[1-(2-metoxi-1-metil-etilcarbamoil)-1-metil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico

Se acopló el ácido 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-2-metil-propiónico con la amina apropiada produciendo el compuesto del título; EM 505,9 m/z (M + 1).

Los siguientes ejemplos se prepararon mediante procedimientos análogos a los descritos anteriormente para el procedimiento general O;

Ejemplo 129 a

(1-{1-metil-2-[(tetrahidropiran-4-ilmetil)amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico

Se hizo reaccionar el éster 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico con la amina apropiada produciendo el compuesto del título; EM 504,6 m/z (M + 1); los diastereómeros se separaron usando condiciones de HPLC quiral (columna OD-H (2,1 x 250 cm); 10 ml/min; 95/5 Heptano/EtOH + DEA al 0,2%)

Ejemplo 130

(1-{2-[(1-hidroxi-ciclohexilmetil)-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se hizo reaccionar el éster 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-etílico del ácido metanosulfónico con la amina apropiada produciendo el compuesto del título; EM 504,6 m/z (M + 1).

Ejemplo 131

(1-{2-[(4-hidroxi-tetrahidropiran-4-ilmetil)-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-

pentanoico

Se hizo reaccionar el éster 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-etílico del ácido metanosulfónico con la amina apropiada produciendo el compuesto del título; EM 506,6 m/z (M + 1).

Ejemplo 132

(1-{2-[(tetrahidro-piran-4-ilmetil)-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se hizo reaccionar el éster 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-etílico del ácido metanosulfónico con la amina apropiada produciendo el compuesto del título; EM 490,5 m/z (M + 1).

Ejemplo 133

(1-{2-[(3-metil-oxetan-3-ilmetil)-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se hizo reaccionar el éster 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-etílico del ácido metanosulfónico con la amina apropiada produciendo el compuesto del título; EM 476,6 m/z (M + 1).

Ejemplo 133 A

(1-{2-[(1-hidroxi-ciclohexilmetil)-amino]-1-metil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-

pentanoico

Se hizo reaccionar el éster 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico con la amina apropiada produciendo el compuesto del título; EM 518,3 m/z (M + 1).

Ejemplo 134

{1-[2-(2-etoxi-etilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico

Se hizo reaccionar el éster 2-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-etílico del ácido metanosulfónico con la amina apropiada produciendo el compuesto del título; EM 464,6 m/z (M + 1).

Ejemplo 135

[1-(3-bencilamino-propil)-1H-imidazol-4-il]amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico

Se hizo reaccionar el éster 3-{4-[2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoilamino]-imidazol-1-il}-propílico del ácido metanosulfónico con la amina apropiada produciendo el compuesto del título; EM 496,3 m/z (M + 1).

Los siguientes ejemplos se prepararon mediante procedimientos análogos a los descritos anteriormente para el procedimiento general B;

Ejemplo 136

(1-{1,1-dimetil-3-[(piridin-2-ilmetil)amino]-propil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico

Se hizo reaccionar la (1-{1,1-dimetil-3-[(piridin-2-ilmetil)-amino]-propil}-1H-imidazol-4-il)amida del ácido 2-amino-pentanoico con 6,8-difluoro-3,4-dihidro-1H-naftalen-2-ona produciendo el compuesto del título; EM 525,5 m/z (M + 1).

Ejemplo 137

{1-[1,1-dimetil-3-((S)-2,2,2-trifluoro-1-fenil-etilamino)propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se hizo reaccionar la {1-[1,1-dimetil-3-(2,2,2-trifluoro-1-fenil-etilamino)propil]-1H-imidazol-4-il}amida del ácido 2-amino-pentanoico con 6,8-difluoro-3,4-dihidro-1H-naftalen-2-ona produciendo el compuesto del título; EM 592,3 m/z (M + 1).

Ejemplo 138

{1-[1,1-dimetil-3-((R)-1-fenil-etilamino)propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico

Se hizo reaccionar la {1-[1,1-dimetil-3-(1-fenil-etilamino)-propil]-1H-imidazol-4-il}amida del ácido 2-amino-pentanoico con 6,8-difluoro-3,4-dihidro-1H-naftalen-2-ona produciendo el compuesto del título; EM 538,6 m/z (M + 1).

Ejemplo 139

{1-[2-((2R,6S)-2,6-dimetilmorfolin-4-il)-1,1-dimetiletil]-1H-imidazol-4-il}amida del ácido (S)-2-(2-trifluorometil-bencilamino)-pentanoico

Se hizo reaccionar la {1-[2-(2,6-dimetilmorfolin-4-il)-1,1-dimetil-etil]-1H-imidazol-4-il}amida del ácido 2-amino-pentanoico con el aldehído apropiado produciendo el compuesto del título; EM 510,5 m/z (M + 1).

Ejemplo 140

{1-[2-((2R,6S)-2,6-dimetilmorfolin-4-il)-1,1-dimetiletil]-1H-imidazol-4-il}amida del ácido (S)-2-{[(2-fluoro-3-trifluorometil-fenil)metil]-amino}pentanoico

Se hizo reaccionar la {1-[2-(2,6-dimetilmorfolin-4-il)-1,1-dimetil-etil]-1H-imidazol-4-il}amida del ácido 2-amino-pentanoico con el aldehído apropiado produciendo el compuesto del título; EM 528,6 m/z (M + 1).

Los siguientes ejemplos se prepararon mediante procedimientos análogos a los descritos anteriormente para la reducción del nitroimidazol apropiado usando el procedimiento general G seguido del acoplamiento con el ácido apropiado usando el procedimiento general A, procedimiento F.

Ejemplo 140 a

(S)-2-[2-(3,5-difluoro-fenil)acetilamino]-N-[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-2-fenilacetamida

Se redujo 1-(2-metil-1-(pirrolidin-1-il)propan-2-il)-4-nitro-1H-imidazol (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) y se acopló con el ácido (S)-2-(2-(3,5-difluorofenil)acetamido)-2-fenilacético produciendo el compuesto del título; EM 496 m/z (M + 1).

Ejemplo 141

(S)-2-[2-(3,5-difluoro-fenil)acetilamino]-N-{1-[2-((2S, 6R)-2,6-dimetil-

morfolin-4-il)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-fenilacetamida

Se redujo 2,6-dimetil-4-[2-metil-2-(4-nitro-imidazol-1-il)-propil]-morfolina (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) y se acopló con el ácido (S)-2-(2-(3,5-difluorofenil)acetamido)-2-fenilacético produciendo el compuesto del título; EM 540 m/z (M + 1).

Ejemplo 142

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1-[2-(2,2-dimetil-propilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-fenilacetamida

Se redujo 2-metil-N-neopentil-2-(4-nitro-1H-imidazol-1-il)propan-1-amina (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) y se acopló con el ácido (S)-2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-3-ilamino)-2-fenilacético produciendo el compuesto del título; EM 524 m/z (M + 1).

Ejemplo 143

(1-indan-1-il-1H-imidazol-4-il)-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico

Se redujo 1-(2,3-dihidro-1H-inden-1-il)-4-nitro-1H-imidazol y se acopló con el ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) produciendo el compuesto del título; EM 453 m/z (M + 1).

Ejemplo 144

[(S)-1-((1S, 2R)-2-hidroxi-indan-1-il)-1H-imidazol-4-il]-amida del ácido (S)- 2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico

Se redujo (1S, 2R)-2,3-dihidro-1-(4-nitro-1H-imidazol-1-il)-1H-inden-2-ol y se acopló con el ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) produciendo el compuesto del título; EM 469 m/z (M + 1).

Ejemplo 145

[(R)-1-((1R, 2S)-2-hidroxi-indan-1-il)-1H-imidazol-4-il]-amida del ácido (S)- 2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico

Se redujo (1R, 2S)-2,3-dihidro-1-(4-nitro-1H-imidazol-1-il)-1H-inden-2-ol y se acopló con el ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) produciendo el compuesto del título; EM 469 m/z (M + 1).

Ejemplo 146

{1-[1-(4-fluorofenil)-2-hidroxi-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico

Se redujo 2-(4-amino-1H-imidazol-1-il)-2-(4-fluorofenil)etanol y se acopló con el ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) produciendo el compuesto del título; EM 475 m/z (M + 1).

Ejemplo 147

{(R)-1-[(R)-1-(4-fluoro-fenil)-2-hidroxi-etil]-1H-imidazol-4-il}-amida del ácido (S)-2- [2-(3,5-difluoro-fenil)acetilamino]pentanoico

Se redujo (R)-2-(4-amino-1H-imidazol-1-il)-2-(4-fluorofenil)etanol y se

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acopló con el ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) produciendo el compuesto del título; EM 475 m/z (M + 1).

Ejemplo 148

[1-(2-hidroximetil-fenil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico

Se redujo (2-(4-nitro-1H-imidazol-1-il)-fenil)metanol y se acopló con el ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) produciendo el compuesto del título; EM 443 m/z (M + 1).

Ejemplo 149

(S)-2-[2-(3,5-difluoro-fenil)acetilamino]-N-{1-[2-(2,2-dimetil-propilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-fenil-acetamida

Se redujo 2-metil-N-neopentil-2-(4-nitro-1H-imidazol-1-il)propan-1-amina (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) y se acopló con el ácido (S)-2-(2-(3,5-difluoro-fenil)acetamido]-2-fenilacético produciendo el compuesto del título; EM 512 m/z (M + 1).

Ejemplo 150

{(S)-1-[2-(2,2-dimetilpropilamino)-1-fenil-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se redujo (S)-2,2-dimetil-N-(2-(4-nitro-1H-imidazol-1-il)-2-feniletil)propan-1-amina y se acopló con el ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-

2-ilamino)-pentanoico (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) produciendo el compuesto del título; EM 538 m/z (M + 1).

Ejemplo 151

{(S)-1-[2-(2,2-dimetilpropilamino)-1-fenil-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

Se redujo (R)-2,2-dimetil-N-(2-(4-nitro-1H-imidazol-1-il)-2-feniletil)propan-1-amina y se acopló con el ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) produciendo el compuesto del título; EM 538 m/z (M + 1).

Ejemplo 152

2-[2-(3,5-difluoro-fenil)acetilamino]-N-{1-[2-(2,2-dimetilpropilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-(4-fluoro-fenil)acetamida

Se redujo 2-metil-N-neopentil-2-(4-nitro-1H-imidazol-1-il)propan-1-amina (Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) y se acopló con el ácido (S)-2-(2-(3,5-difluorofenil)acetamido)-2-(4-fluorofenil)acético produciendo el compuesto del título; EM 530 m/z (M + 1).

Ejemplo 153

2-[2-(3,5-difluoro-fenil)acetilamino]-N-{1-[2-(2,2-dimetilpropilamino)-1,1- dimetil-etil]-1H-imidazol-4-il}-2-piridin-3-il-acetamida

Se redujo 2-metil-N-neopentil-2-(4-nitro-1H-imidazol-1-il)propan-1-amina

(Documento U. S. nº de serie 11/078.898 presentado el 11 de marzo de 2005) y se acopló con el ácido (S)-2-(2-(3,5-difluorofenil)acetamido)-2-(piridin-3-il)acético produciendo el compuesto del título; EM 513 m/z (M + 1).

Los siguientes ejemplos se prepararon mediante procedimientos análogos a los descritos usando el procedimiento general B

Ejemplo 154

(1-{2-[(2,2-dimetil-propilamino)-metil]-fenil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

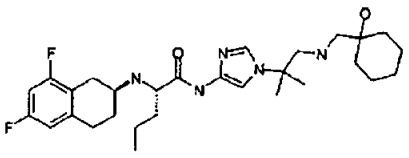
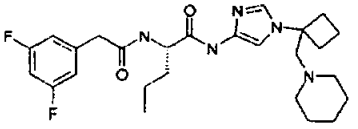
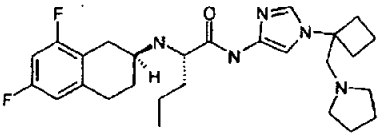
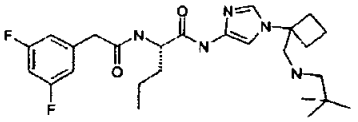
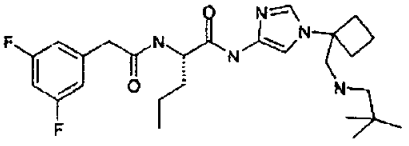
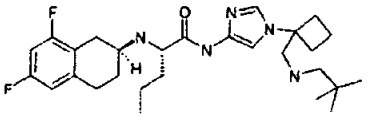
Se trató (2S)-2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-3-ilamino)-N-(1-(2-formilfenil)-1H-imidazol-4-il)pentanamida con la amina apropiada produciendo el compuesto del título: EM 524 m/z (M + 1).

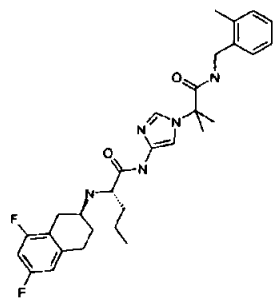
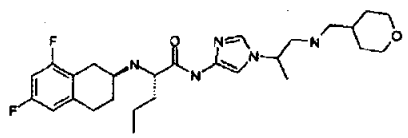
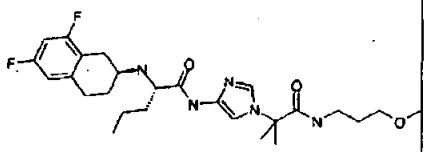
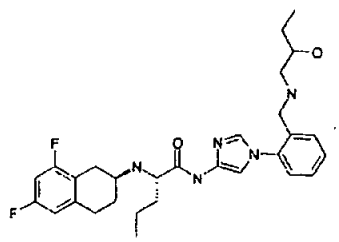
Ejemplo 155

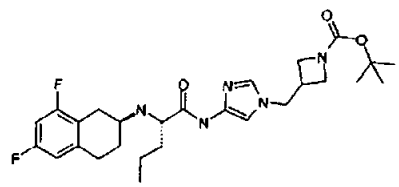
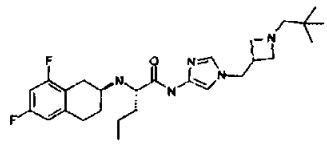
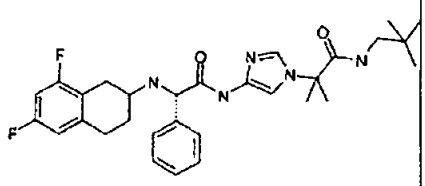
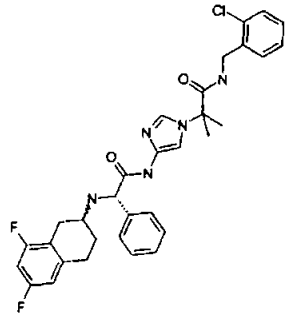
(1-{2-[(2-hidroxi-butilamino)-metil]-fenil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

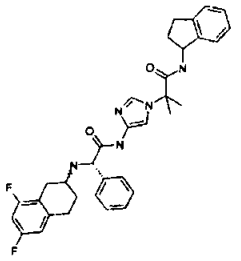
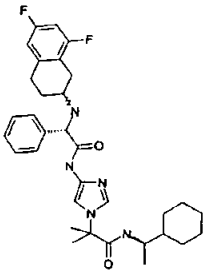
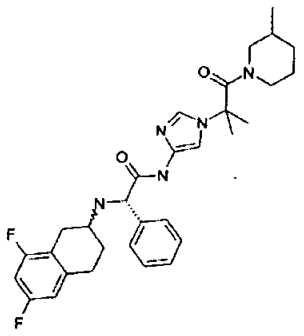
Se trató (2S)-2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-3-ilamino)-N-(1-(2-formilfenil)-1H-imidazol-4-il)pentanamida con la amina apropiada produciendo el compuesto del título: EM 526 m/z (M + 1).

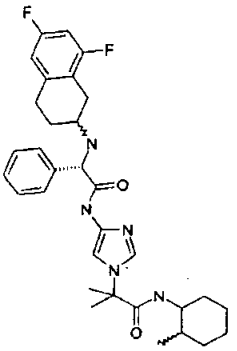
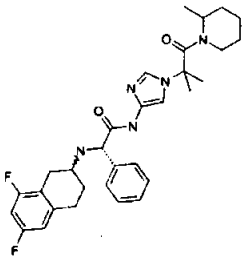
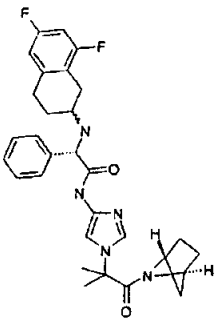
Los siguientes ejemplos se prepararon mediante procedimientos análogos a los descritos anteriormente.

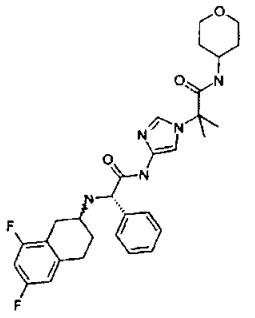
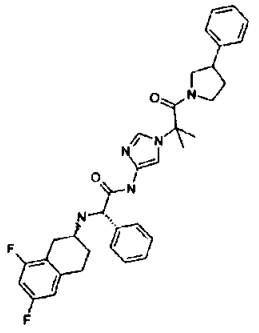
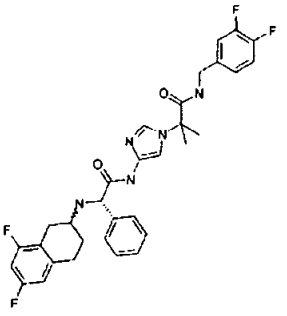
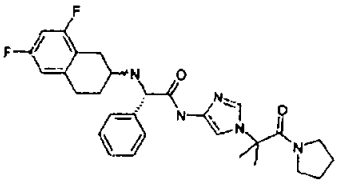
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
156		M + 1 = 532,6	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(1-hidroxiciclohexil)metil]amino}-1,1-dimetiletil)-1H-imidazol-4-il]-L-norvalinamida
157		M + 1 = 488,5	N-2-[(3,5-difluorofenil)acetil]-N-{1-[1-(piperidin-1-ilmetil)ciclobutil]-1H-imidazol-4- il}-L-norvalinamida
158		M + 1 = 486,5	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[1-(pirrolidin-1-ilmetil)ciclobutil]-1H-imidazol- 4-il}-L-norvalinamida
159		M + 1 = 490,1	N-2-[(3,5-difluorofenil)acetil]-N-[1-(1-{[(2,2-dimetilpropil) amino]metil}ciclobutil)-1H-imidazol-4-il]-L-norvalinamida
160		M + 1 = 490,1	N-2-[(3,5-difluorofenil)acetil]-N-[1-(1-{[(2,2-dimetilpropil) amino]metil}ciclobutil)-1H-imidazol-4-il]-L-norvalinamida
161		M + 1 = 502,6	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(1-{[(2,2-dimetilpropil)amino]metil}ciclobutil)-1H-imidazol-4-il]-L-norvalinamida

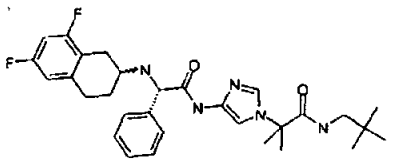
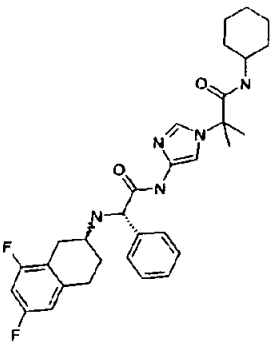
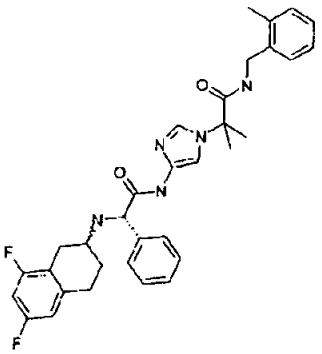
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
162		M + 1 = 538,26	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{1,1-dimetil-2-[(2-metilbencil)amino]-2-oxoetil}-1H-imidazol-4-il)-L-norvalinamida
163		M + 1 = 504,1	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{1-metil-2-[(tetrahidro-2H-piran-4-ilmetil)amino]etil}-1H-imidazol-4-il)-L-norvalinamida
164		M + 1 = 506,52	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(3-metoxipropil)amino]-1,1-dimetil-2-oxoetil}-1H-imidazol-4-il)-L-norvalinamida
165		M + 1 = 526,64	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2-hidroxibutil)amino]-metil}fenil)-1H-imidazol-4-il]-L-norvalinamida

Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
166		M + 1 = 518,5	3-{[4-({N-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalil}amino)-1H-imidazol-1-il]metil}azetidina-1-carboxilato de terc-butilo
167		M + 1 = 488,5	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{[1-(2,2-dimetilpropil)azetidin-3-il]metil}-1H-imidazol-4-il)-L- norvalinamida
168		M + 1 = 538,65	2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-N-(2,2-dimetilpropil)-2-metilpropanamida
169		M + 1 = 593,09	N-(2-clorobencil)-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-2-metilpropanamida

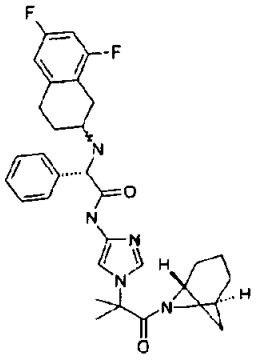
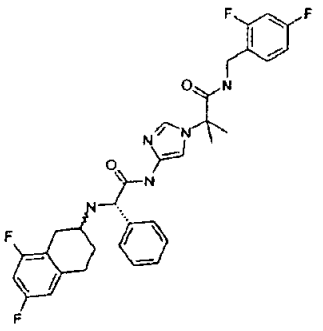
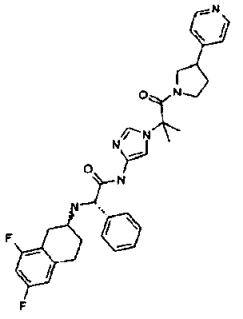
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
170		M + 1 = 584,68	2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-N-(2,3-dihidro-1H-inden-1-il)-2-metilpropanamida
171		M + 1 = 578,72	N-[(1R)-1-ciclohexiletil]-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-2-metilpropanamida
172		M + 1 = 550,66	(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-N-{1-[1,1-dimetil-2-(3-metilpiperidin-1-il)-2-oxoetil]-1H-imidazol-4-il}-2-fenilacetamida

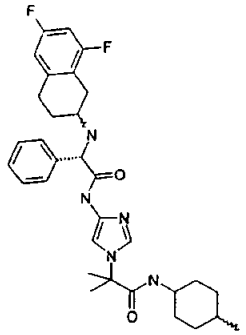
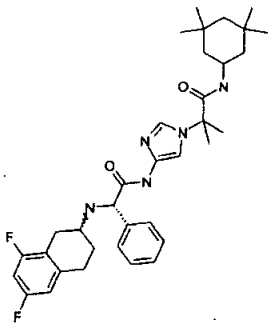
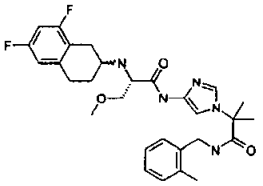
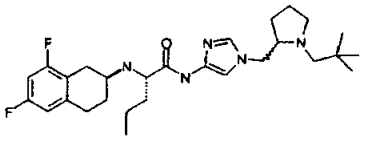
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
173		M + 1 = 564,69	2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-2-metil-N-(2-metilciclohexil) propanamida
174		M + 1 = 550,66	(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-N-{1-[1,1-dimetil-2-(2-metilpiperidin-1-il)-2-oxoetil]-1H-imidazol-4-il}-2-fenilacetamida
175		M + 1 = 548,65	(2S)-N-(1-{2-[(1R,4S)-2-azabiciclo[2.2.1]hept-2-il]-1,1-dimetil-2-oxoetil}-1H-imidazol-4-il)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2- fenilacetamida

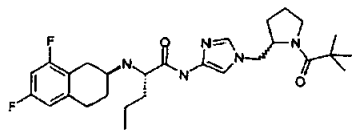
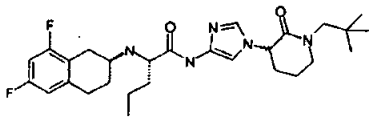
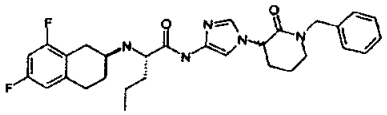
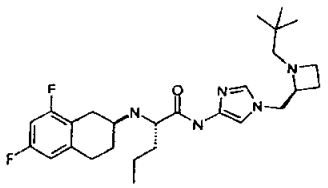
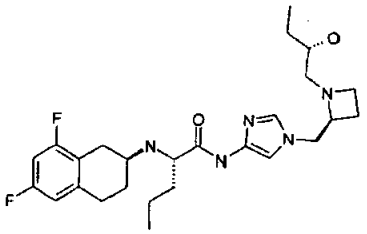
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
176		M + 1 = 552,64	2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-2-metil-N-(tetrahidro-2H-piran-4-il)propanamida
177		M + 1 = 598,71	(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-N-{1-[1,1-dimetil-2-oxo-2-(3-fenilpirrolidin-1-il)etil]-1H-imidazol-4-il}-2-fenilacetamida
178		M + 1 = 594,62	N-(3,4-difluorobencil)-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-2-metilpropanamida
179		M + 1 = 522,61	(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-N-[1-(1,1-dimetil-2-oxo-2-pirrolidin-1-iletil)-1H-imidazol-4-il]-2-fenilacetamida

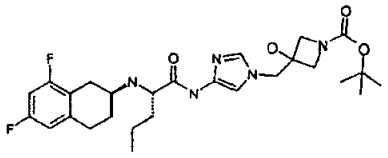
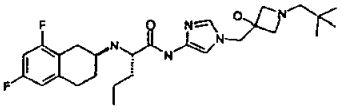
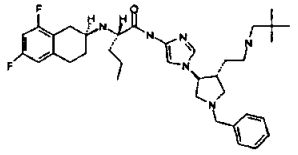
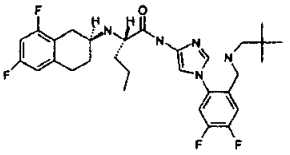
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
180		M + 1 = 538,65	2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-N-(2,2-dimetilpropil)-2-metilpropanamida
181		M + 1 = 550,66	N-ciclohexil-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-2-metilpropanamida
182		M + 1 = 572,67	2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-2-metil-N-(2-metilbencil)propanamida

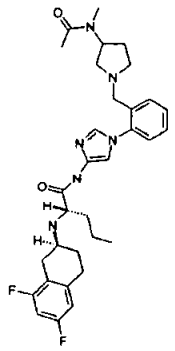
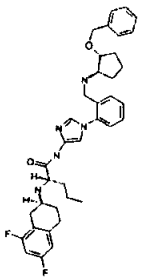
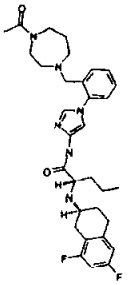
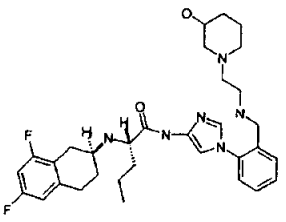
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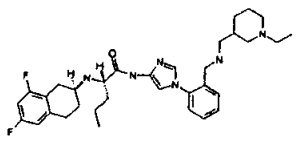
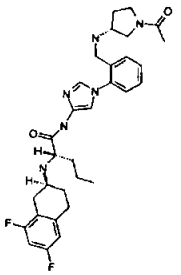
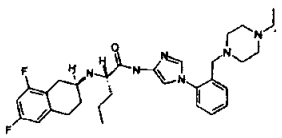
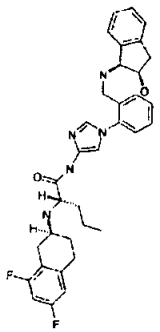
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
183		M + 1 = 562,67	(2S)-N-(1-{2-[(1S,5R)-6-azabiciclo[3.2.1]oct-6-il]-1,1-dimetil-2-oxoetil}-1H-imidazol-4-il)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetamida
184		M + 1 = 594,62	N-(2,4-difluorobencil)-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-2-metilpropanamida
185		M + 1 = 599,69	(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-N-{1-[1,1-dimetil-2-oxo-2-(3-piridin-4-ilpirrolidin-1-il)etil]-1H-imidazol-4-il}-2-fenilacetamida

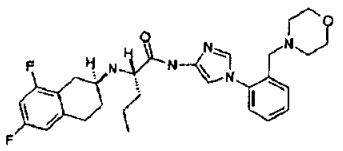
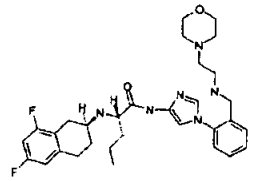
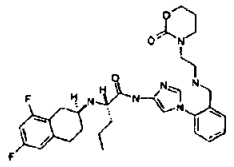
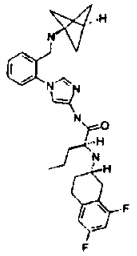
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
186		M + 1 = 564,69	2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-2-metil-N-(4-metilciclohexil) propanamida
187		M + 1 = 606,77	2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-2-metil-N-(3,3,5,5-tetrametilciclohexil)propanamida
188		M + 1 = 540,04	N-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)-N-(1-{1,1-dimetil-2-[(2-metilbencil)amino]-2-oxoetil}-1H-imidazol-4-il)-O-metil-L-serinamida
189		M + 1 = 502,5	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{[1-(2,2-dimetilpropil)pirrolidin-2-il]metil}-1H-imidazol-4-il)-L-norvalinamida

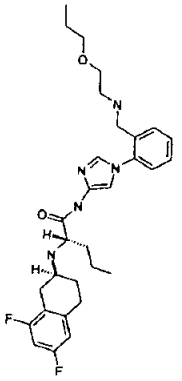
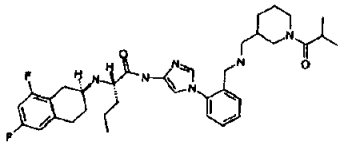
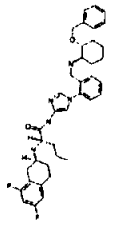
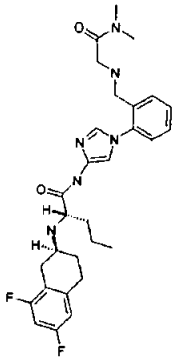
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
190		M + 1 = 516,5	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{[1-(2,2-dimetilpropanoil)pirrolidin-2-il]metil}-1H-imidazol-4-il)-L-norvalinamida
191		M + 1 = 516,4	(2S)-2-{[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]amino}-N-{1-[1-(2,2-dimetilpropil)-2-oxopiperidin-3-il]-1H-imidazol-4-il}pentanamida
192		M + 1 = 536,3	(2S)-N-[1-(1-bencil-2-oxopiperidin-3-il)-1H-imidazol-4-il]-2-{[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]amino}pentanamida
193		M + 1 = 488,4	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{[(2S)-1-(2,2-dimetilpropil)azetidin-2-il]metil}-1H-imidazol-4-il)-L-norvalinamida
194		M + 1 = 490,3	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-({(2S)-1-[(2S)-2-hidroxibutil]azetidin-2-il}metil)-1H-imidazol-4-il]-L-norvalinamida

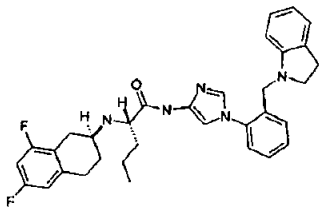
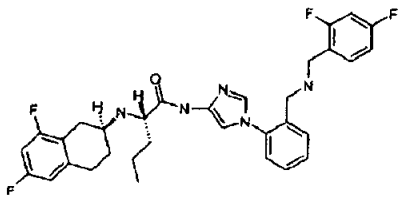
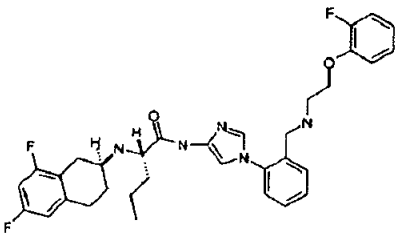
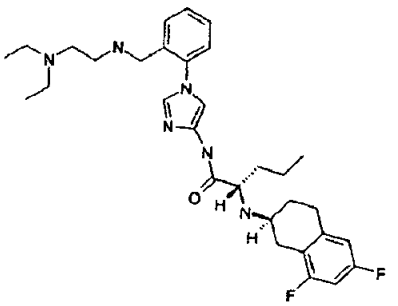
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
195		M + 1 = 534,4	3-{[4-({N-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalil}amino)-1H-imidazol-1-il]metil}-3-hidroxiazetidina-1-carboxilato de terc-butilo
196		M + 1 = 504,4	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{[1-(2,2-dimetilpropil)-3-hidroxiazetidin-3-il]-metil}-1H-imidazol-4-il)-L-norvalinamida
197		M + 1 = 621,83	N-{1-[(3S,4R)-1-bencil-4-{2-[(2,2-dimetilpropil)amino]etil}pirrolidin-3-il]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
198		M + 1 = 560,65	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2,2-dimetilpropil)amino]metil}-4,5-difluorofenil)-1H-imidazol-4-il]-L-norvalinamida

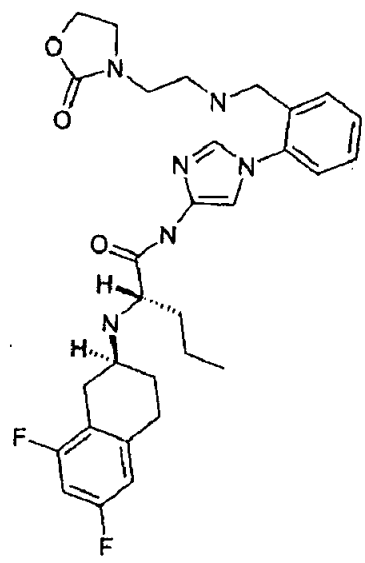
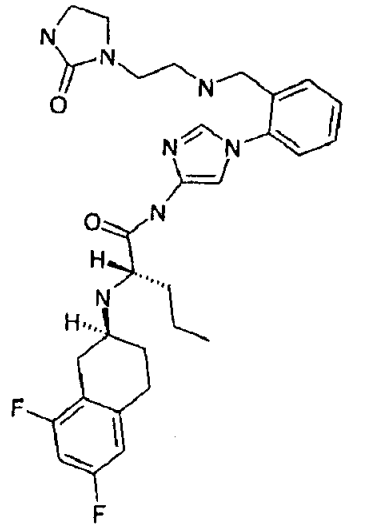
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
199		M + 1 = 579,7	N-{1-[2-({3-[acetil(metil)amino]pirrolidin-1-il}-metil)fenil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
200		M + 1 = 628,78	N-{1-[2-({[(1R,2R)-2-(benciloxi)ciclopentil]amino}metil)fenil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
201		M + 1 = 579,7	N-(1-{2-[(4-acetil-1,4-diazepan-1-il)metil]fenil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
202		M + 1 = 581,72	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(3-hidroxipiperidin-1-il)etil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida

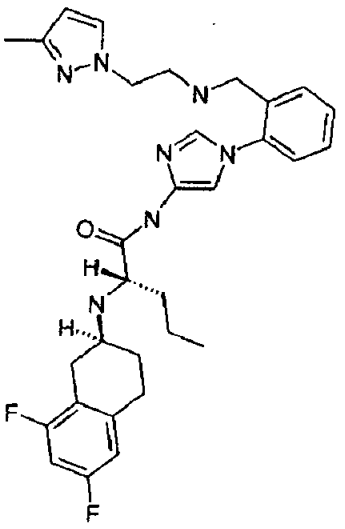
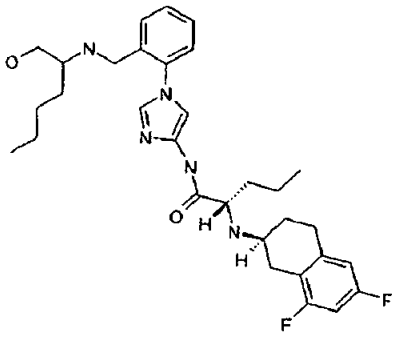
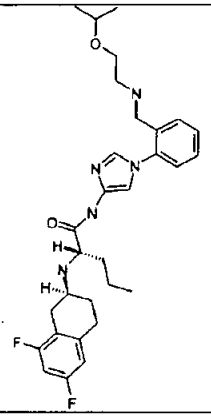
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
203		M + 1 = 579,75	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1-etilpiperidin-3-il)metil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
204		M + 1 = 565,68	N-{1-[2-({[(3R)-1-acetilpirrolidin-3-il]amino}metil)fenil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
205		M + 1 = 551,69	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(4-etilpiperazin-1-il)metil]fenil}-1H-imidazol- 4-il)-L-norvalinamida
206		M + 1 = 586,7	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1S,2R)-2-hidroxi-2,3-dihidro-1H-inden-1-il]amino}metil)fenil]-1H-imidazol- 4-il}-L-norvalinamida

Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
207		M + 1 = 524,63	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-(morfolin-4-ilmetil)fenil]-1H-imidazol-4-il}-L-norvalinamida
208		M + 1 = 567,69	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2-morfolin-4-iletil)amino]metil}fenil)-1H-imidazol- 4-il]-L-norvalinamida
209		M + 1 = 581,68	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(2-oxo-1,3-oxazinan-3-il)etil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
210		M + 1 = 520,64	N-(1-{2-[(biciclo[1.1.1]pent-1-ilamino)metil]fenil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida

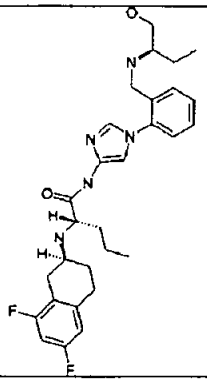
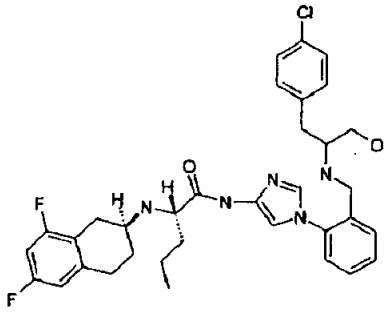
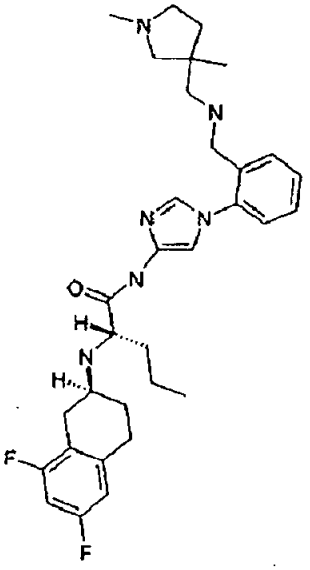
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
211		M + 1 = 540,67	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2-propoxietil)amino]metil}fenil)-1H-imidazol- 4-il]-L-norvalinamida
212		M + 1 = 621,78	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1-isobutirilpiperidin-3-il)metil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
213		M + 1 = 642,8	N-{1-[2-({[(1R,2R)-2-(benciloxi)ciclohexil]amino}metil)fenil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
214		M + 1 = 539,64	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(dimetilamino)-2-oxoetil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida

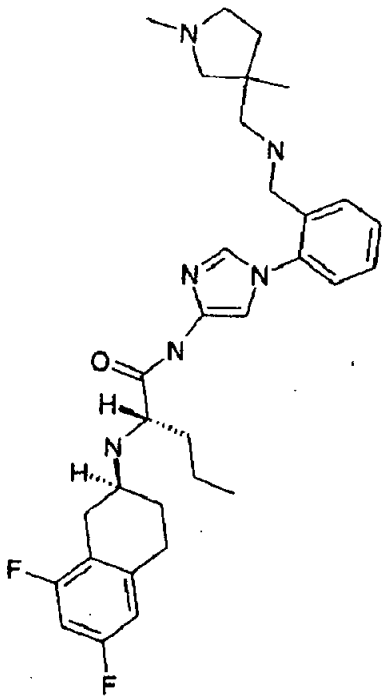
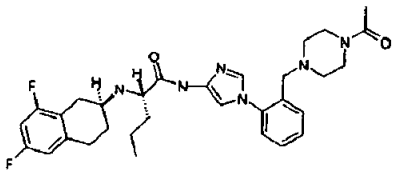
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
215		M + 1 = 556,67	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-(2,3-dihidro-1H-indol-1-ilmetil)fenil]-1H-imidazol-4-il}-L-norvalinamida
216		M + 1 = 580,64	N-[1-(2-{[(2,4-difluorobencil)amino]metil}fenil)-1H-imidazol-4-il]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
217		M + 1 = 592,67	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(2-fluorofenoxi)etil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
218		M + 1 = 553,71	N-{1-[2-({[2-(dietilamino)etil]amino}metil)fenil]-1H-imidazol-4-il]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida

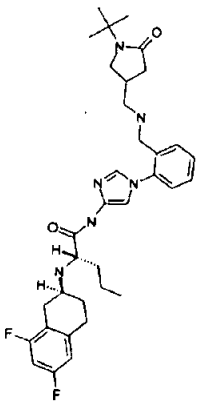
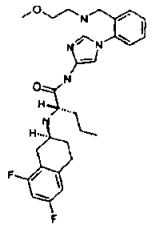
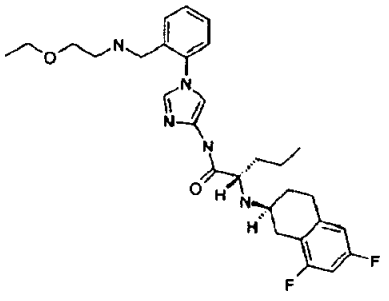
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
219		M + 1 = 567,65	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(2-oxo-1,3-oxazolidin-3-il)etil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
220		M + 1 = 566,67	N-2-{(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(2-oxoimidazolidin-1-il)etil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida

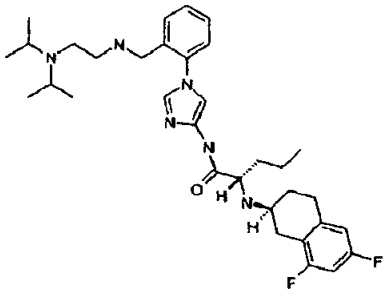
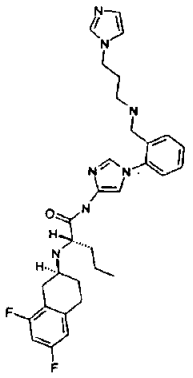
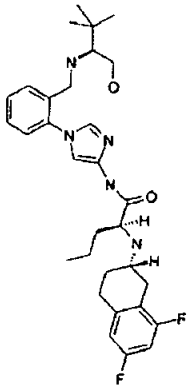
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
221		M + 1 = 562,68	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(3-metil-1H-pirazol-1-il])etil]amino]-metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
222		M + 1 = 554,69	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[1-(hidroximetil)pentil]amino}metil)fenil]-1H-imidazol-4- il}-L-norvalinamida
223		M + 1 = 540,67	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2-isopropoxietil)amino]metil}fenil)-1H-imidazol-4- il]-L-norvalinamida

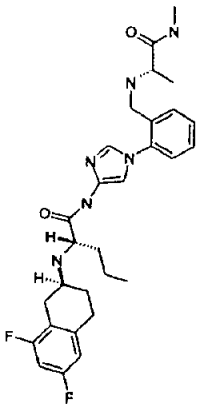
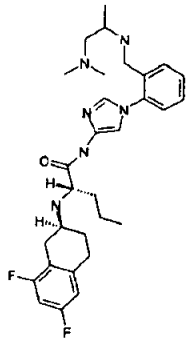
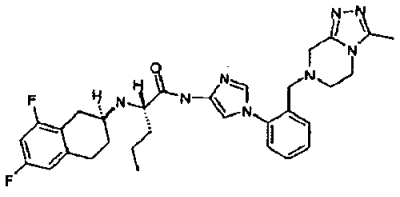
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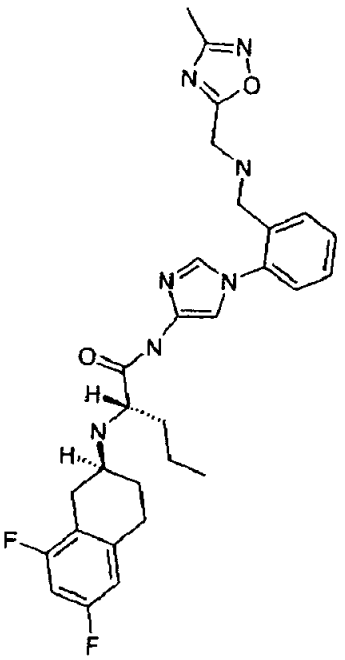
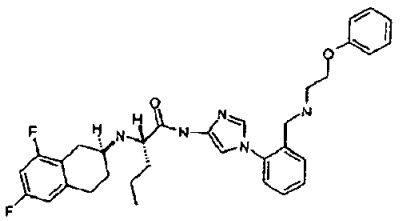
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
224		M + 1 = 526,64	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1R)-1-(hidroximetil)propil]amino} metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
225		M + 1 = 623,16	N-{1-[2-({[1-(4-clorobencil)-2-hidroxietil]amino}metil)fenil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
226		M + 1 = 565,72	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1,3-dimetilpirrolidin-3-il)metil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida

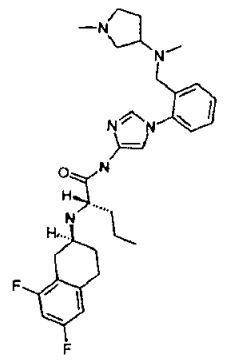
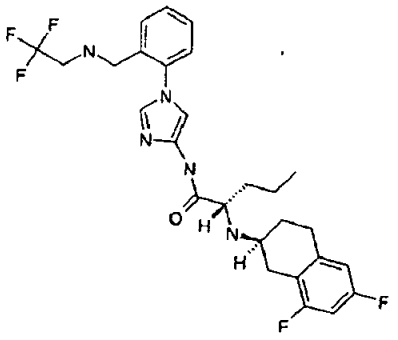
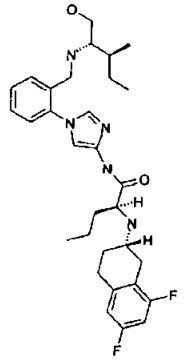
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
227		M + 1 = 565,72	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1,3-dimetilpirrolidin-3-il)metil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
228		M + 1 = 565,68	N-(1-{2-[(4-acetilpiperazin-1-il)metil]fenil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida

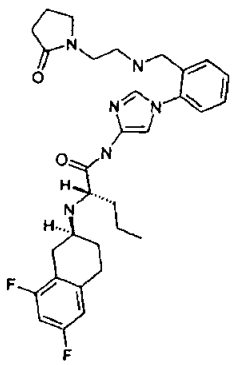
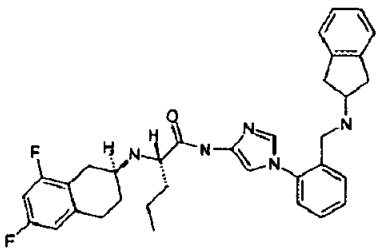
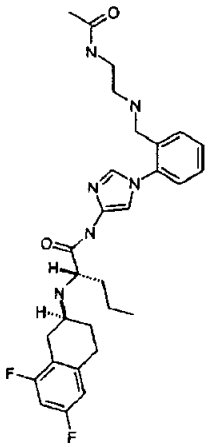
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
229		M + 1 = 607,76	N-{1-[2-({[(1-terc-butil-5-oxopirrolidin-3-il)metil]amino}metil)fenil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
230		M + 1 = 512,61	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2-metoxietil)amino]metil}fenil)-1H-imidazol- 4-il]-L-norvalinamida
231		M + 1 = 526,64	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2-etoxietil)amino]metil}fenil)-1H-imidazol- 4-il]-L-norvalinamida

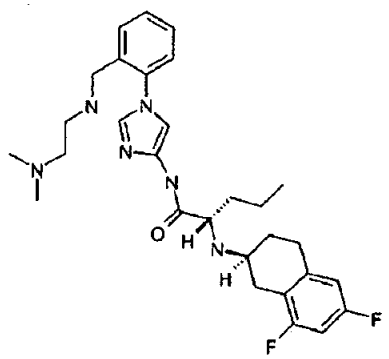
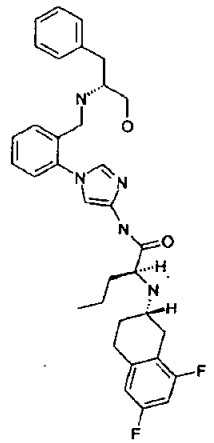
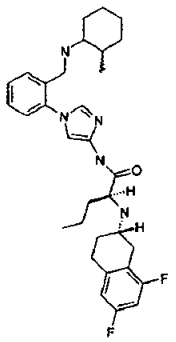
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
232		M + 1 = 581,76	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(diisopropilamino)etil]amino}metil) fenil]-1H-imidazol-4-il}-L-norvalinamida
233		M + 1 = 562,68	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[3-(1H-imidazol-1-il)propil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
234		M + 1 = 554,69	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1S)-1-(Hidroximetil)-2,2-dimetilpropil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida

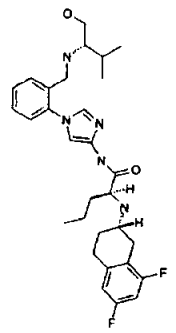
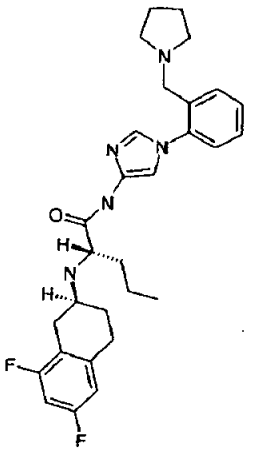
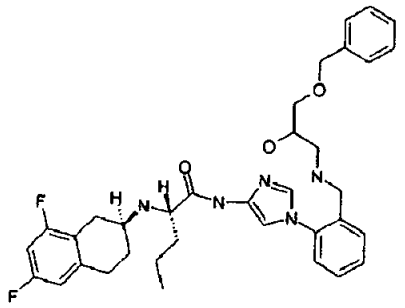
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
235		M + 1 = 539,64	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1S)-1-metil-2-(metilamino)-2-oxoetil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
236		M + 1 = 539,68	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(dimetilamino)-1-metiletil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
237		M + 1 = 575,68	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(3-metil-5,6-dihidro[1,2,4]triazolo[4,3-a]pirazin-7(8H)-il)metil]fenil}-1H-imidazol-4-il)-L-norvalinamida

Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
238		M + 1 = 550,62	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(3-metil-1,2,4-oxadiazol-5-il)metil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
239		M + 1 = 574,68	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2-fenoxietil)amino]metil}fenil)-1H-imidazol-4-il]-L-norvalinamida

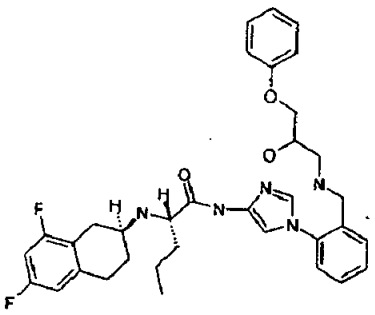
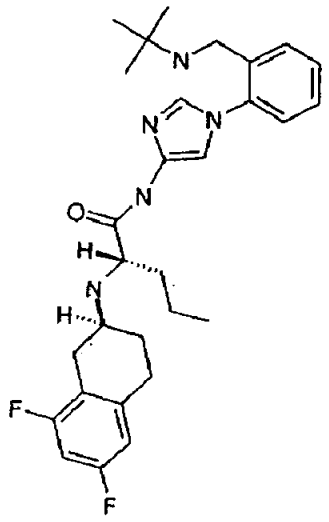
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
240		M + 1 = 551,69	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[metil(1-metilpirrolidin-3-il)amino]metil}fenil)-1H-imidazol-4-il]-L-norvalinamida
241		M + 1 = 536,56	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2,2,2-trifluoroetil)amino]metil}fenil)-1H-imidazol-4-il]-L-norvalinamida
242		M + 1 = 554,69	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1S, 2S)-1-(hidroximetil)-2-metilbutil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida

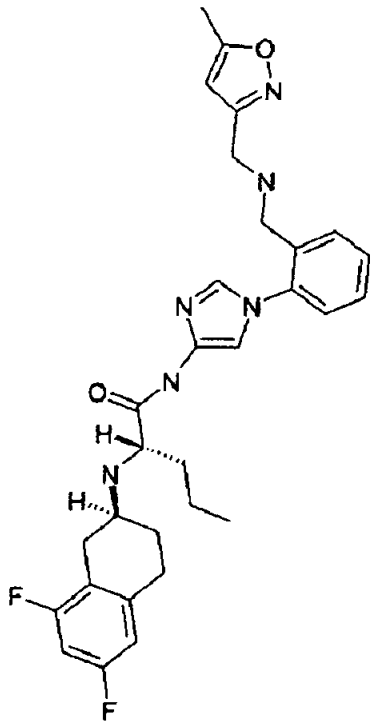
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
243		M + 1 = 565,68	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(2-oxopirrolidin-1-il)etil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
244		M + 1 = 570,7	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(2,3-dihidro-1H-inden-2-ilamino)metil]fenil}-1H-imidazol-4-il)-L-norvalinamida
245		M + 1 = 539,64	N-{1-[2-({[2-(acetilamino)etil]amino}metil)fenil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida

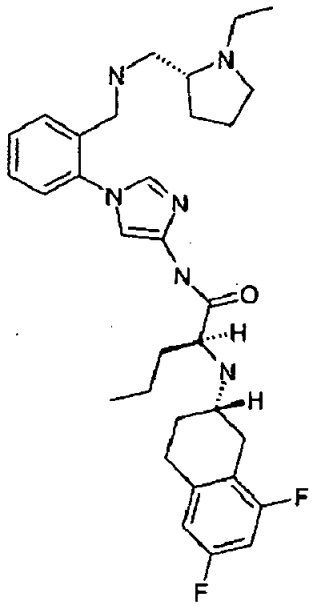
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
246		M + 1 = 525,66	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(dimetilamino)etil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
247		M + 1 = 588,71	N-{1-[2-({[(1R)-1-bencil-2-hidroxietil]amino}metil)fenil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
248		M + 1 = 550,71	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2-metilciclohexil)amino]metil}fenil)-1H-imidazol-4-il]-L-norvalinamida

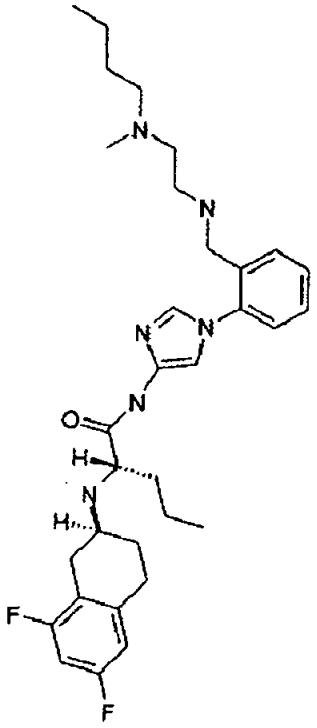
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
249		M + 1 = 540,67	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1S)-1-(hidroximetil)-2-metilpropil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
250		M + 1 = 508,63	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-(pirrolidin-1-ilmetil)fenil]-1H-imidazol-4-il}-L-norvalinamida
251		M + 1 = 618,74	N-{1-[2-({[3-(benciloxi)-2-hidroxipropil]amino}metil)fenil]-1-H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida

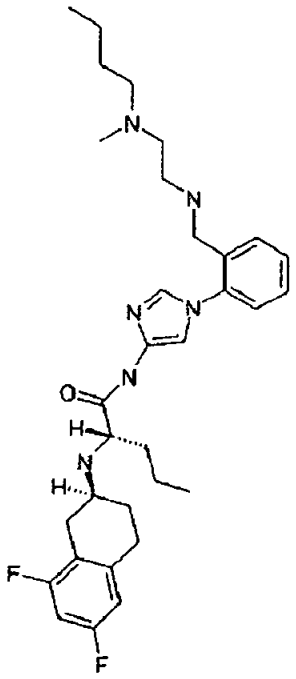
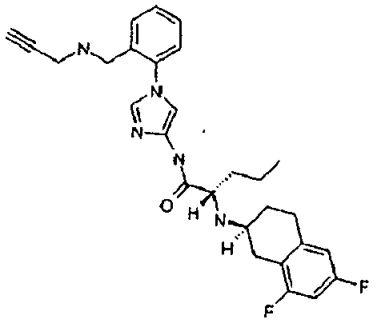
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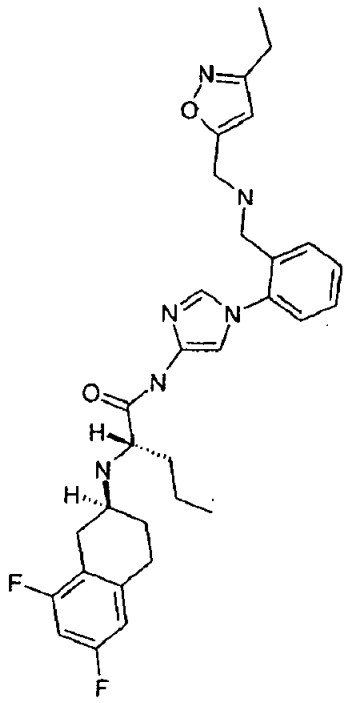
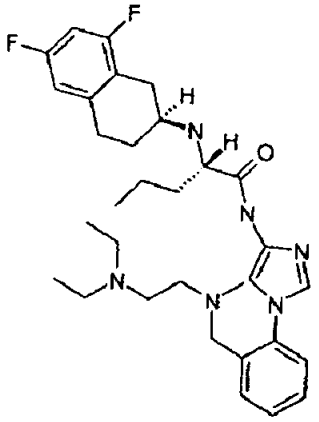
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
252		M + 1 = 604,71	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2-hidroxi-3-fenoxipropil) amino]metil}fenil)-1H-imidazol-4-il]-L-norvalinamida
253		M + 1 = 510,64	N-(1-{2-[(terc-butilamino)metil]fenil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida

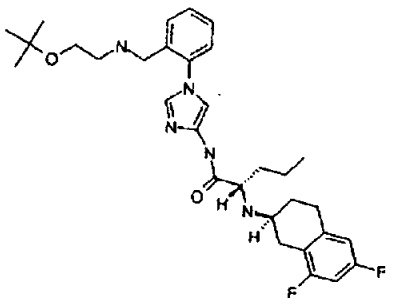
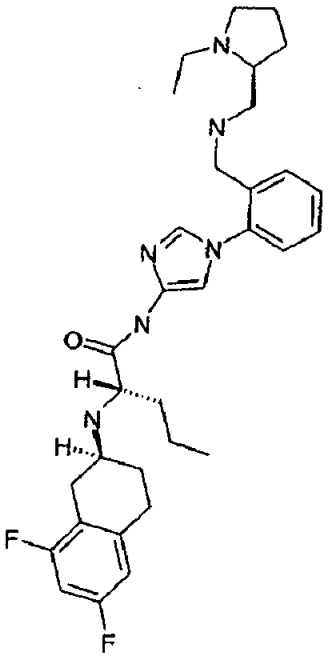
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
254		M + 1 = 549,64	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(5-metilisoxazol-3-il)metil] amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida

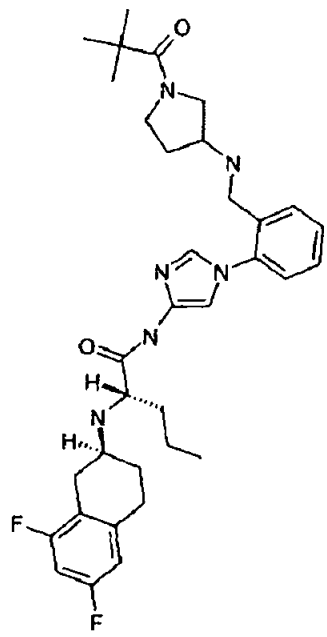
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
255		M + 1 = 565,72	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[({[(2R)-1-etilpirrolidin-2-il]metil}amino)metil]fenil}-1H-imidazol-4-il)-L-norvalinamida

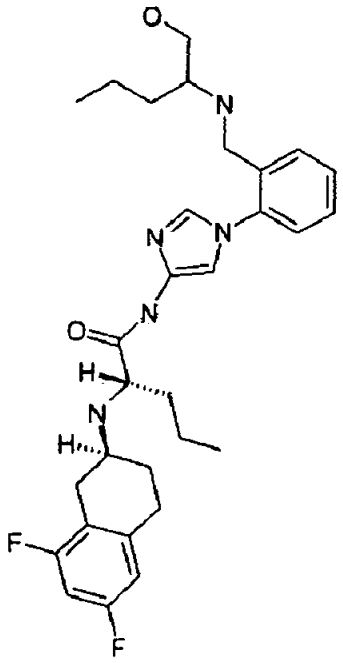
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
256		M + 1 = 567,74	N-(1-{2-[({2-[butil(metil)amino]etil}amino)metil] fenil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida

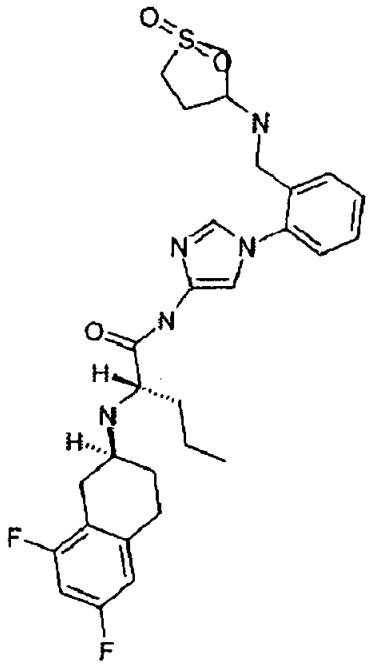
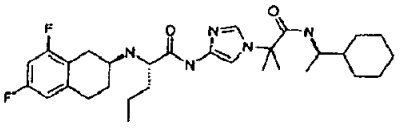
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
257		M + 1 = 567,74	N-(1-{2-[({2-[butil(metil)amino]etil}amino)metil]fenil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
258		M + 1 = 492,58	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(prop-2-in-1-ilamino)metil]fenil}-1H-imidazol-4-il)-L-norvalinamida

Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
259		M + 1 = 563,66	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(3-etilisoxazol-5-il)metil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
260		M + 1 = 567,74	N-{1-[2-({[2-(dietilamino)etil](metil)amino}metil)fenil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida

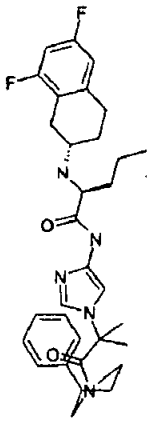
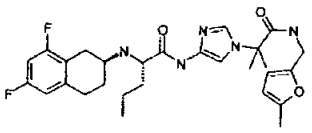
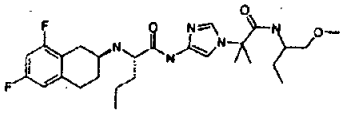
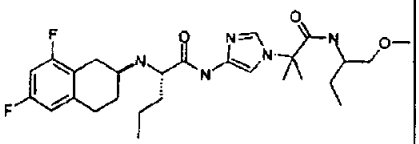
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
261		M + 1 = 554,69	N-[1-(2-{[(2-terc-butoxietil)amino]metil}fenil)-1H-imidazol-4-il]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
262		M + 1 = 565,72	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[({[(2S)-1-etilpirrolidin-2-il]metil}amino)metil]fenil}-1H-imidazol-4-il)-L-norvalinamida

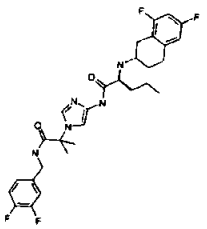
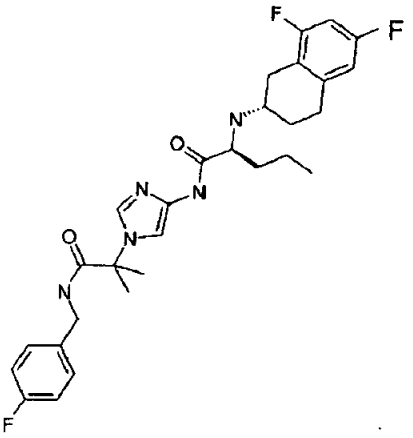
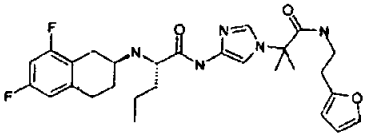
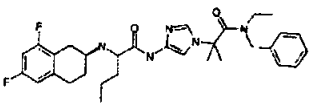
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
263		M + 1 = 607,76	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[1-(2,2-dimetilpropanoil)pirrolidin-3-il]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida

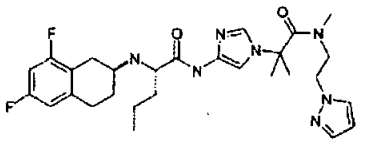
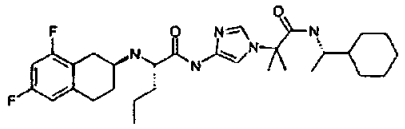
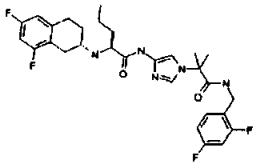
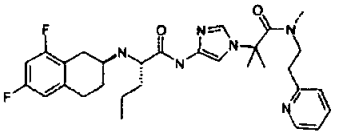
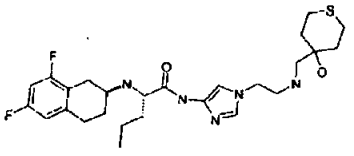
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
264		M + 1 = 540,67	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[1-(hidroximetil)butil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida

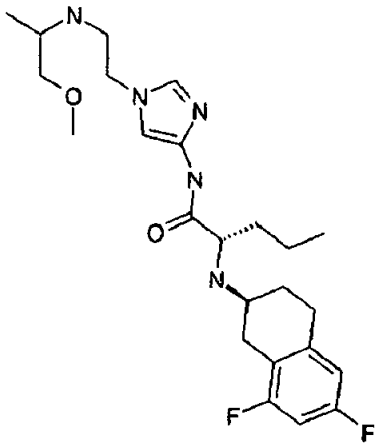
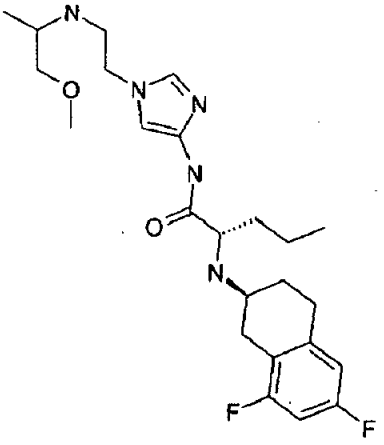
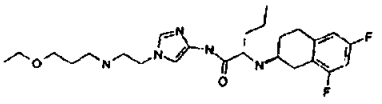
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
265		M + 1 = 572,69	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(1,1-dióxidotetrahidro-3-tienil)amino]metil}fenil)-1H-imidazol-4-il]-L-norvalinamida
266		M + 1 = 544,28	N-[1-(2-{[(1R)-1-ciclohexiletil]amino}-1,1-dimetil-2-oxoetil)-1H-imidazol-4-il]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida

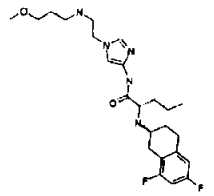
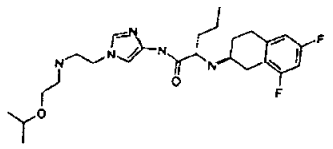
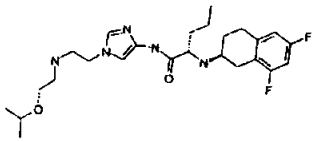
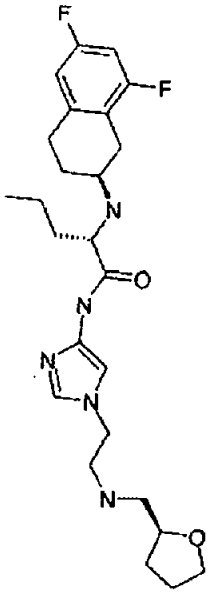
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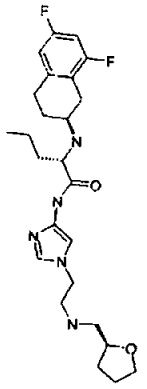
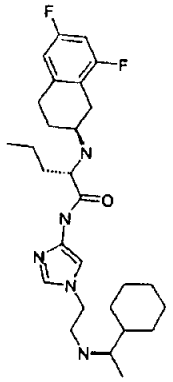
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
267		M + 1 = 564,29	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[1,1-dimetil-2-oxo-2-(3-fenilpirrolidin-1-il)etil]-1H-imidazol-4-il}-L-norvalinamida
268		M + 1 = 528,25	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(1,1-dimetil-2-{[(5-metil-2-furil)metil]amino}-2-oxoetil)-1H-imidazol-4-il]-L- norvalinamida
269		M + 1 = 520,3	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[1-(metoximetil)propil]amino}-1,1-dimetil-2-oxoetil)-1H-imidazol-4-il]-L-norvalinamida
270		M + 1 = 520,28	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[1-(metoximetil)propil]amino}-1,1-dimetil-2-oxoetil)-1H-imidazol-4-il]-L-norvalinamida

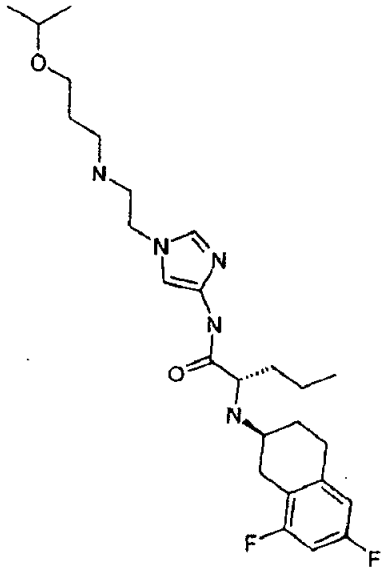
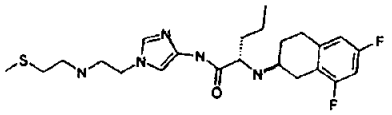
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
271		M + 1 = 560,22	N-(1-{2-[(3,4-difluorobencil)amino]-1,1-dimetil-2-oxoetil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
272		M + 1 = 542,25	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(4-fluorobencil)amino]-1,1-dimetil-2-oxoetil}-1H-imidazol-4-il)-L-norvalinamida
273		M + 1 = 528,28	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[2-(2-furil)etil]amino}-1,1-dimetil-2-oxoetil)-1H-imidazol-4-il]-L-norvalinamida
274		M + 1 = 552,12	N-(1-{2-[bencil(etil)amino]-1,1-dimetil-2-oxoetil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida

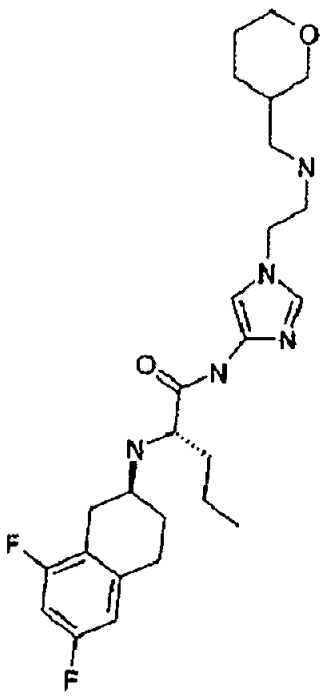
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
275		M + 1 = 548,25	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(1,1-dimetil-2-{metil[2-(1H-pirazol-1-il)etil]amino}-2-oxoetil)-1H-imidazol-4-il]-L-norvalinamida
276		M + 1 = 544,31	N-[1-(2-{[(1S)-1-ciclohexiletil]amino}-1,1-dimetil-2-oxoetil)-1H-imidazol-4-il]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
277		M + 1 = 560,2	N-(1-{2-[(2,4-difluorobencil)amino]-1,1-dimetil-2-oxoetil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
278		M + 1 = 553,23	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{1,1-dimetil-2-[metil(2-piridin-2-iletil)amino]-2-oxoetil}-1H-imidazol-4-il)-L- norvalinamida
279		datos no disponibles	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(4-hidroxitetrahidro-2H-tiopiran-4-il)metil]amino}etil)-1H-imidazol-4-il]-L-norvalinamida

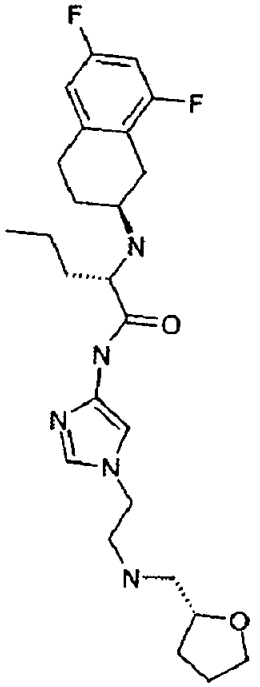
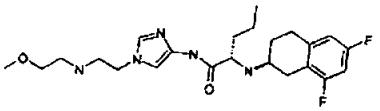
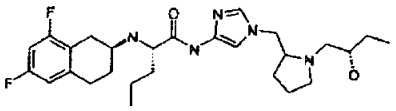
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
280		M + 1 = 464,2	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(2-metoxi-1-metiletil)amino]etil}-1H-imidazol-4-il)-L-norvalinamida
281		datos no disponibles	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(2-metoxi-1-metiletil)amino]etil}-1H-imidazol-4-il)-L-norvalinamida
282		datos no disponibles	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(3-etoxipropil)amino]etil}-1H-imidazol-4-il)-L-norvalinamida

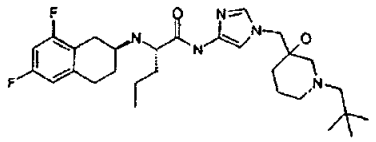
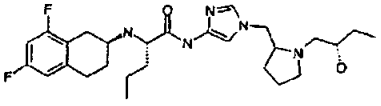
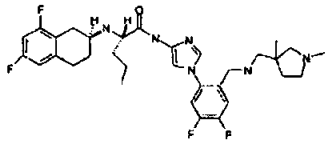
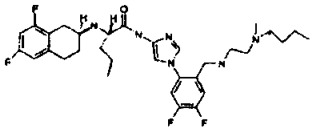
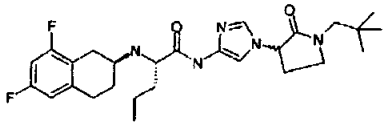
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
283		M + 1 = 464,3	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(3-metoxipropil)amino]etil}-1H-imidazol-4-il)-L-norvalinamida
284		M + 1 = 478,3	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(2-isopropoxietil)amino]etil}-1H-imidazol-4-il)-L-norvalinamida
285		datos no disponibles	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(2-isopropoxietil)amino]etil}-1H-imidazol-4- il)-L-norvalinamida
286		M + 1 = 476,3	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2S)-tetrahidrofuran-2-ilmetil]amino}etil)-1H-imidazol-4-il]-L-norvalinamida

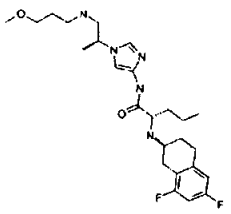
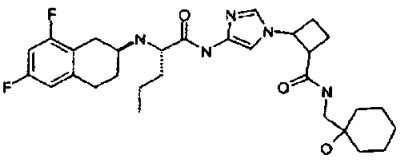
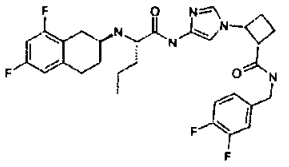
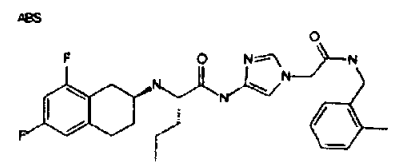
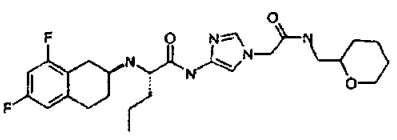
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
287		datos no disponibles	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2S)-tetrahidrofuran-2-ilmetil]amino}etil)-1H-imidazol-4-il]-L-norvalinamida
288		datos no disponibles	N-[1-(2-{[(1R)-1-ciclohexiletil]amino}etil)-1H-imidazol-4-il]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida

Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
289		datos no disponibles	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(3-isopropoxipropil)amino]etil}-1H-imidazol-4- il)-L-norvalinamida
290		datos no disponibles	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[2-(metiltio)etil]amino}etil)-1H-imidazol-4-il]-L-norvalinamida

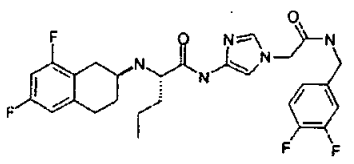
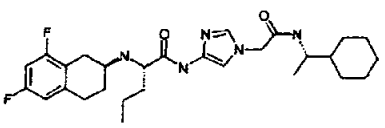
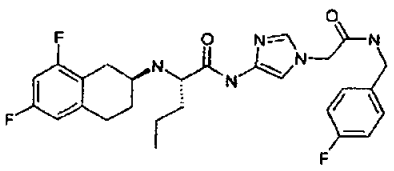
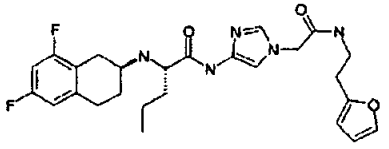
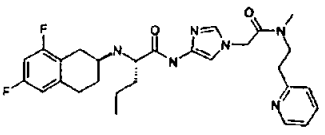
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
291		datos no disponibles	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(tetrahidro-2H-piran-3-ilmetil)amino]etil}-1H-imidazol-4-il)-L-norvalinamida

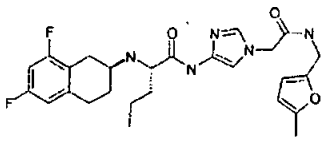
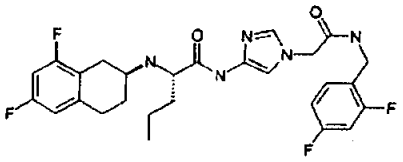
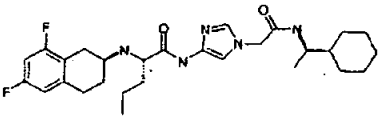
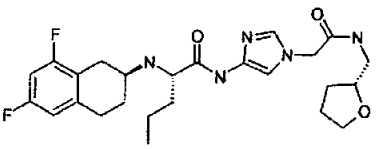
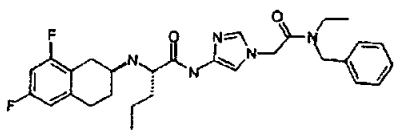
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
292		datos no disponibles	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2R)-tetrahidrofuran-2-ilmetil]amino}etil)-1H-imidazol-4-il]-L-norvalinamida
293		datos no disponibles	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(2-metoxietil)amino]etil}-1H-imidazol-4-il)-L-norvalinamida
294		M + 1 = 504,4	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-({1-[(2S)-2-hidroxibutil]pirrolidin-2-il}metil)-1H-imidazol-4-il]-L-norvalinamida

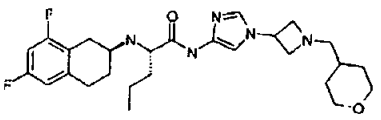
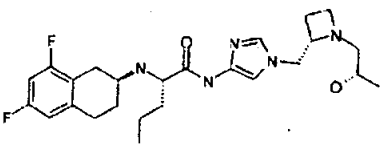
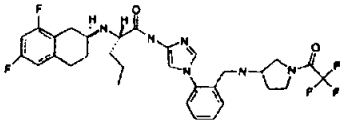
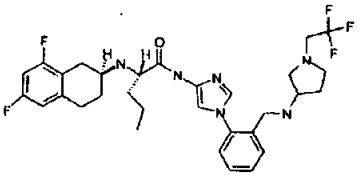
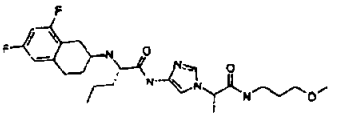
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
295		M + 1 = 532,5	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{[1-(2,2-dimetilpropil)-3-hidroxipiperidin-3-il]metil}-1H-imidazol-4-il)-L-norvalinamida
296		M + 1 = 504,4	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-({1-[(2S)-2-hidroxibutil]pirrolidin-2-il}metil)-1H-imidazol-4-il]-L-norvalinamida
297		M + 1 = 601,7	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1,3-dimetilpirrolidin-3-il)metil]amino}metil)-4,5-difluorofenil]-1H-imidazol-4-il}-L-norvalinamida
298 *		M + 1 = 603,72	N-(1-{2-[({2-[butil(metil)amino]etil}amino)metil]-4,5- difluorofenil}-1H-imidazol-4-il)-N-2- [(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
299		M + 1 = 502,3	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[1-(2,2-dimetilpropil)-2-oxopirrolidin-3-il]-1H-imidazol-4-il}-L-norvalinamida

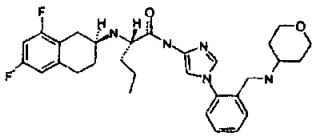
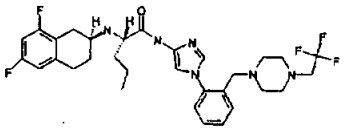
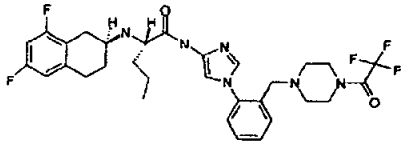
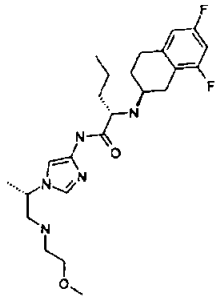
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
300		M + 1 = 478,3	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{(1S)-2-[(3-metoxipropil)amino]-1-metiletil}-1H- imidazol-4-il)-L-norvalinamida
301		M + 1 = 558,3	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1-hidroxiciclohexil)metil]amino}carbonil) ciclobutil]-1H-imidazol-4-il}-L-norvalinamida
302		M + 1 = 572,29	N-[1-(2-{[(3,4-difluorobencil)amino]carbonil} ciclobutil)-1H-imidazol-4-il]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
303		M + 1 = 510,23	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(2-metilbencil)amino]-2-oxoetil}-1H-imidazol-4-il)-L-norvalinamida
304		M + 1 = 504,26	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-oxo-2-[(tetrahidro-2H-piran-2-ilmetil)amino]etil}-1H-imidazol-4-il)-L-norvalinamida

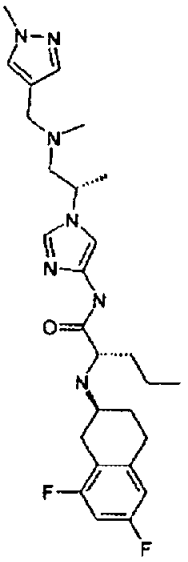
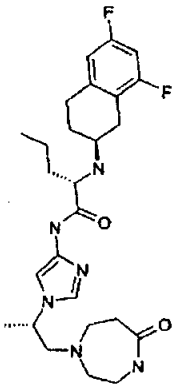
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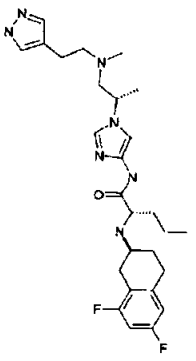
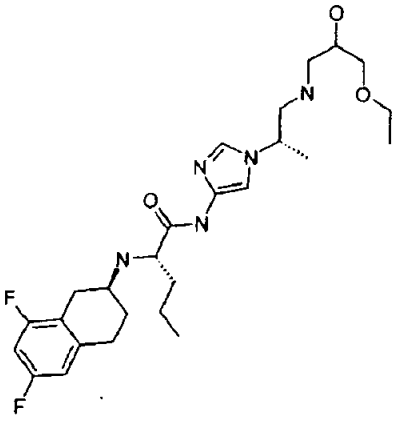
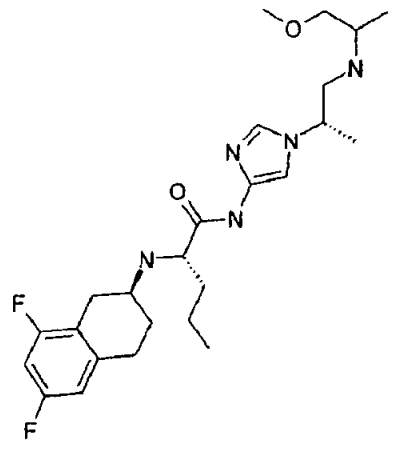
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
305		M + 1 = 532,22	N-(1-{2-[(3,4- difluorobencil)amino]-2-oxoetil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida.
306		M + 1 = 516,29	N-[1-(2-{[(1S)-1-ciclohexiletil]amino}-2-oxoetil)-1H-imidazol-4-il]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
307		M + 1 = 514,22	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(4-fluorobencil)amino]-2-oxoetil}-1H-imidazol-4-il)-L-norvalinamida
308		M + 1 = 500,22	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[2-(2-furil)etil]amino}-2-oxoetil)-1H-imidazol-4-il]-L-norvalinamida
309		M + 1 = 525,23	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[metil(2-piridin-2-iletil)amino]-2-oxoetil}-1H-imidazol-4-il)-L-norvalinamida

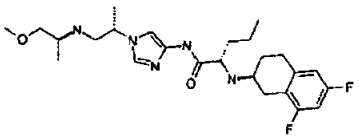
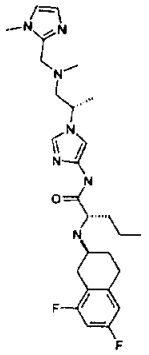
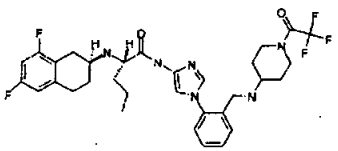
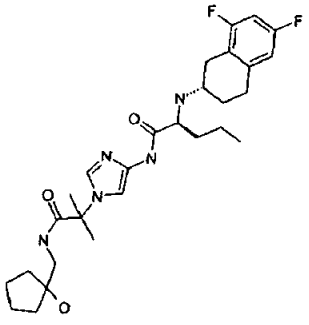
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
310		M + 1 = 500,22	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(5-metil-2-furil)metil]amino}-2-oxoetil)-1H-imidazol-4-il]-L-norvalinamida
311		M + 1 = 532,21	N-(1-{2-[(2,4-difluorobencil)amino]-2-oxoetil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
312		M + 1 = 516,3	N-[1-(2-{[(1R)-1-ciclohexiletil]amino}-2-oxoetil)-1H-imidazol-4-il]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
313		M + 1 = 490,26	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-oxo-2-{[(2R)-tetrahidrofuran-2-ilmetil]amino}etil)-1H-imidazol-4-il]-L-norvalinamida
314		M + 1 = 524,27	N-(1-{2-[bencil(etil)amino]-2-oxoetil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida

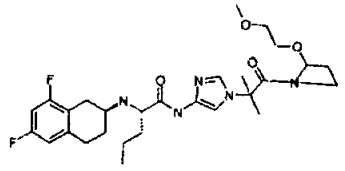
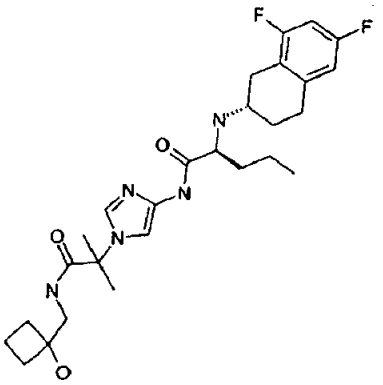
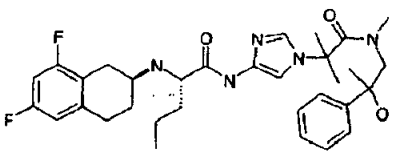
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
315		M + 1 = 502,2	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[1-(tetrahidro-2H-piran-4-ilmetil)azetidin-3-il]-1H-imidazol-4-il}-L-norvalinamida
316		M + 1 = 476,3	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-({(2S)-1-[(2S)-2-hidroxipropil]azetidin-2-il}metil)-1H-imidazol-4-il]-L-norvalinamida
317		M + 1 = 619,65	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[1-(trifluoroacetil)pirrolidin-3-il]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
318		M + 1 = 605,66	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[1-(2,2,2-trifluoroetil)pirrolidin-3-il]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
319		M + 1 = 492,1	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(3-metoxipropil)amino]-1-metil-2-oxoetil}-1H-imidazol-4-il)-L-norvalinamida

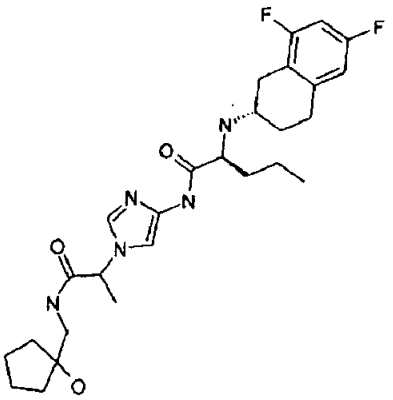
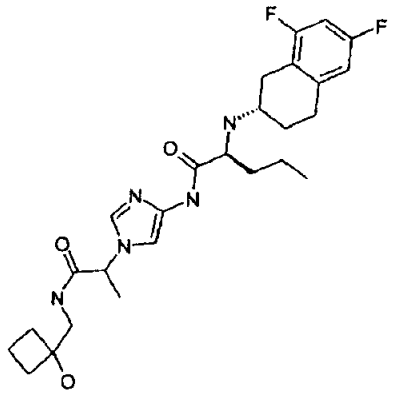
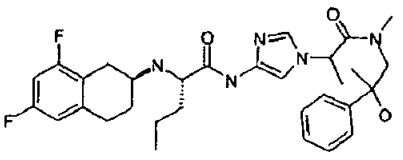
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
320		M + 1 = 538,65	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(tetrahidro-2H-piran-4-ilamino)metil]fenil}-1H-imidazol-4-il)-L-norvalinamida
321		M + 1 = 605,66	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[4-(2,2,2-trifluoroetil)piperazin-1-il]metil}fenil)-1H-imidazol-4-il]-L-norvalinamida
322		M + 1 = 619,65	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[4-(trifluoroacetil)piperazin-1-il]metil}fenil)-1H-imidazol-4-il]-L-norvalinamida
323		M + 1 = 465,19	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{(1S)-2-[(2-metoxietil)amino]-1-metiletil}-1H-imidazol-4-il)-L-norvalinamida

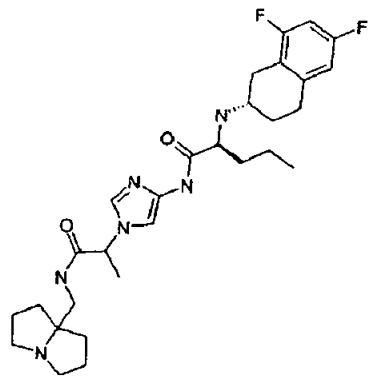
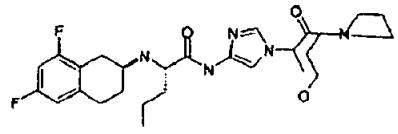
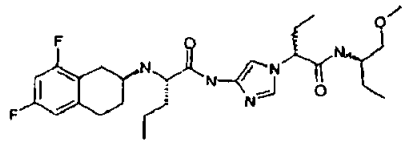
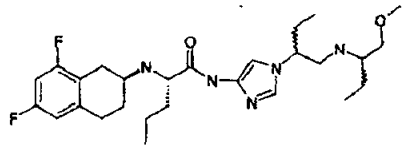
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
324		M + 1 = 514,25	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[(1S)-1-metil-2-{metil[(1-metil-1H-pirazol-4-il)metil]amino}etil]-1H-imidazol-4-il}-L-norvalinamida
325		M + 1 = 503,14	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[(1S)-1-metil-2-(5-oxo-1,4-diazepan-1-il)etil]-1H-imidazol-4-il}-L-norvalinamida

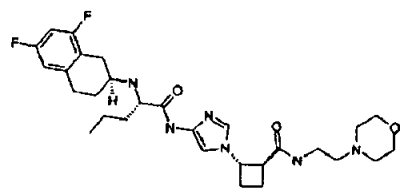
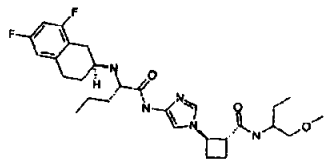
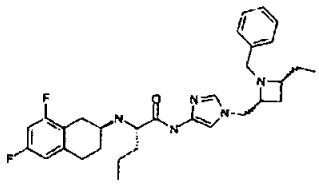
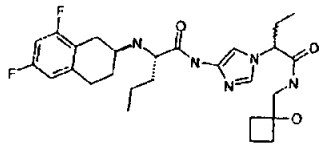
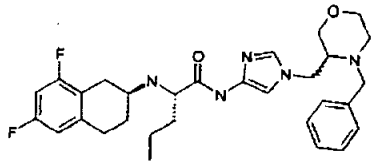
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
326		M + 1 = 514,25	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[(1S)-1-metil-2-{metil[2-(1H-pirazol-4-il)etil]amino}etil]-1H-imidazol-4-il}-L-norvalinamida
327		M + 1 = 508,34	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{(1S)-2-[(3-etoxi-2-hidroxipropil)amino]-1-metiletil}-1H-imidazol-4-il)-L-norvalinamida
328		M + 1 = 478,28	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{(1S)-2-[(2-metoxi-1-metiletil)amino]-1-metiletil}-1H-imidazol-4-il)-L-norvalinamida

Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
329		M + 1 = 478,22	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[(1S)-2-{[(1S)-2-metoxi-1-metiletil]amino}-1-metiletil]-1H-imidazol-4-il}-L-norvalinamida
330		M + 1 = 514,14	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[(1S)-1-metil-2-{metil[(1-metil-1H-imidazol-2-il)metil]amino}etil]-1H-imidazol-4-il}-L-norvalinamida
331		M + 1 = 633,67	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[1-(trifluoroacetil)piperidin-4-il]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida
332		M + 1 = 532,4	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(1-hidroxiciclopentil)metil]amino}-1,1-dimetil-2-oxoetil)-1H-imidazol-4-il]-L-norvalinamida

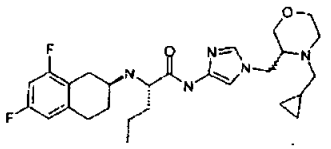
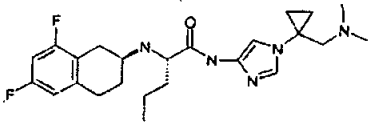
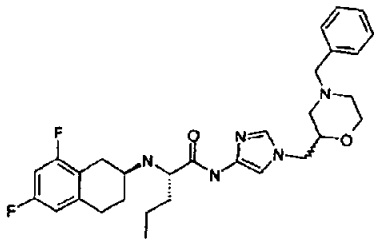
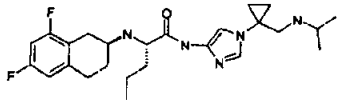
Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
333		M + 1 = 575,95	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[4-(2-metoxietoxi)piperidin-1-il]-1,1-dimetil-2-oxoetil}-1H-imidazol-4-il)-L-norvalinamida
334		M + 1 = 518,23	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(1-hidroxiciclobutil)metil]amino}-1,1-dimetil-2-oxoetil)-1H-imidazol-4-il]-L-norvalinamida
335		M + 1 = 582,29	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(2-hidroxi-2-fenilpropil)(metil)amino]- 1,1-dimetil-2-oxoetil}-1H-imidazol-4- il)-L-norvalinamida

Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
336		M + 1 = 518,22	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(1-hidroxiciclopentil)metil]amino}-1-metil-2-oxoetil)-1H-imidazol-4-il]-L-norvalinamida
337		M + 1 = 504,17	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(1-hidroxiciclobutil)metil]amino}-1-metil-2-oxoetil)-1H-imidazol-4-il]-L-norvalinamida
338		M + 1 = 568,23	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(2-hidroxi-2-fenilpropil)(metil)amino]-1-metil-2-oxoetil}-1H-imidazol-4-il)-L-norvalinamida

Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
339		M + 1 = 543,21	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{1-metil-2-oxo-2-[(tetrahidro-1H-pirrolizin-7a(5H)-ilmetil)amino]etil}-1H-imidazol-4-il)-L-norvalinamida
340		M + 1 = 532,21	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[2-(2-hidroxietil)piperidin-1-il]-1-metil-2-oxoetil}-1H-imidazol-4-il)-L-norvalinamida
341		M + 1 = 520,2	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[1-({[1-(metoximetil)propil]amino}carbonil) propil]-1H-imidazol-4-il}-L-norvalinamida
342		M + 1 = 506,1	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[1-({[1-(metoximetil)propil]amino}metil) propil]-1H-imidazol-4-il}-L-norvalinamida

Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
343		M + 1 = 559,1	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[(1S,2S)-2-{[(2-morfolin-4-iletil)amino]carbonil}ciclobutil]-1H-imidazol-4-il}-L-norvalinamida
344		M + 1 = 532,1	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[(1R, 2R)-2-({[1-(metoximetil)propil] amino}carbonil)ciclobutil]-1H-imidazol-4-il}-L-norvalinamida
345		M + 1 = 536,1	N-{1-[(1-bencil-4-etilazetidin-2-il)metil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
346		M + 1 = 518,2	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[1-({[(1-hidroxiciclobutil)metil]amino}carbonil) propil]-1H-imidazol-4-il}-L-norvalinamida
347		M + 1 = 432	N-{1-[(4-bencilmorfolin-3-il)metil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida

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Ej	Estructura	Datos de EM o RMN	Nombre IUPAC
348		M + 1 = 502	N-(1-{[4-(ciclopropilmetil)morfolin-3-il]metil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
349		M + 1 = 446,0	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{1-[(dimetilamino)metil]ciclopropil}-1H-imidazol-4-il)-L-norvalinamida
350		M + 1 = 538	N-{1-[(4-bencilmorfolin-2-il)metil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida
351		M + 1 = 460,0	N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{1-[(isopropilamino)metil]ciclopropil}-1H-imidazol-4-il)-L-norvalinamida

Ejemplo 352

Los siguientes compuestos se preparan utilizando los procedimientos descritos anteriormente:

{1-[2-(3-etoxi-propilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

[1-(2-fluoro-bencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(3-fluoro-bencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(4-metilbencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(4-metoxibencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro- fenil)acetilamino]-pentanoico;

[1-(4-terc-butil-bencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro- fenil)acetilamino]-pentanoico;

[1-(1-hidroximetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

[1-(2-hidroximetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

[1-(1-pirrolidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-((R)-1-ciclohexil-etilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[2-((R)-1-ciclohexil-etilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2- (2,4-difluoro-fenil)-2-hidroxietilamino]-pentanoico;

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2- (3,4-difluoro-fenil)-2-hidroxietilamino]-pentanoico;

(1-{1,1-dimetil-2-[(tetrahidro-piran-4-ilmetil)-amino]-etil}-1H-imidazol-4-il)-

amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1,1-dimetil-2-[(tetrahidro-piran-4-ilmetil)-amino]etil}-1H-imidazol-4-il)-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[3-((S)-1-fenil-etilamino)-butil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

[1-(3-metil-oxetan-3-ilmetil)-1H-imidazol-4-il]-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

[1-(3-metil-oxetan-3-ilmetil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1-H-imidazol-4-il]amida del ácido (S)-2- [2- (3,5-difluoro-fenil)-2-hidroxietilamino]-pentanoico;

{1-[2-((2R,6S)-2,6-dimetilmorfolin-4-il)-1,1-dimetiletil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(2,4-difluorofenil)-2-hidroxi-etilamino]-pentanoico;

{1-[2-(octahidro-pirazino[1,2-a]azepin-2-il)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-([1,4]-dioxan-2-ilmetil-metilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(2-metoxi-1-metil-etilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3-oxo-piperazin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

[1-(2-bencilamino-etil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro- fenil)acetilamino]-pentanoico;

{1-[2-(3-butoxi-propilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-

(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-((1R,2S)-2-hidroximetil-ciclohexilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[(4aS, 8aS)-2-(octahidro-isoquinolin-2-il)etil]-1H-imidazol-4-il}amida del ácido 2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3-isopropoxi-propilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(octahidro-isoquinolin-2-il)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3,4,5,6-tetrahidro-2H-[4,4']bipiridinil-1-il)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(2-hidroxi-2-fenil-etilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2- (3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(indan-1-ilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(bencil-metilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(indan-2-ilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3,4-dihidro-1H-isoquinolin-2-il)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(2-propoxi-etilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3-bencil-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3-piridin-2-il-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2- (3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(metil-piridin-4-ilmetil-amino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2- [2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

(1-{2-[(2-metanosulfonil-etil)metil-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2- [2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(2-terc-butoxi-etilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2- (3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3-piridin-4-il-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2- (3,5-difluoro-fenil)acetilamino]-pentanoico,

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido (S)-2-[(1- hidroxiciclohexilmetil)amino]-pentanoico;

(S)-2-[2-(3,5-difluoro-fenil)acetilamino]-N-[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-2-fenilacetamida;

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1-H-imidazol-4-il]amida del ácido (S)-2- (diciclopropilmetil-amino)-pentanoico;

{1-[3-((R)-1-fenil-etilamino)propil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{2-[(1-hidroxi-ciclohexilmetil)-amino]-1,1-dimetil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(S)-2-[2-(3,5-difluoro-fenil)acetilamino]-N-{1-[2-((2S,6R)-2,6-dimetil-morfolin-4-il)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-fenilacetamida;

(1-{2-[(4-hidroxi-tetrahidro-piran-4-ilmetil)-amino]-1,1-dimetil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-

ilamino)-pentanoico;

[1-(1-dimetilaminometil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

[1-(1-piperidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

[1-(1-morfolin-4-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

(1-{1-[((2R,6S)-2,6-dimetil-morfolin-4-il)metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

(1-{1-[(2,2,2-trifluoro-etilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

(1-{1-[((R)-1-ciclohexil-etilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

[1-(1-hidroximetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

[1-(1-pirrolidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-[(2,2-dimetil-propilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1-[2-(2,2-dimetil-propilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-fenil-acetamida;

{1-[1-(4-trifluorometilfenil)etil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1-(4-trifluorometil-fenil)-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(2-metoxi-2-metil-propilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

(1-{1,1-dimetil-2-[(3-metiloxetan-3-ilmetil)-amino]etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

{1-[2-(ciclohexilmetil-amino)-1,1-dimetil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)- pentanoico;

(1-{1-metil-2-[(tetrahidropiran-4-ilmetil)amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-indan-1-il-1H-imidazol-4-il)-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico;

[(S)-1-((1S, 2R)-2-hidroxi-indan-1-il)-1H-imidazol-4-il]-amida del ácido (S)- 2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico;

[(R)-1-((1R, 2S)-2-hidroxi-indan-1-il)-1H-imidazol-4-il]-amida del ácido (S)- 2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico;

[1-(2-pirrolidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico;

[1-(2-pirrolidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)pentanoico;

{1-[1-(4-fluorofenil)-2-hidroxi-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico;

{1-[3-(3-metil-bencilamino)-propil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(2-hidroxi-2-fenil-etilamino)-propil]-1H-imidazol-4-il}-amida del ácido

(S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(2-cloro-bencilamino)-propil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(3,4-dihidro-1H-isoquinolin-2-il)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(indan-2-ilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(1-metoximetil-propilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(4-cloro-bencilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

{1-[3-(2-metilbencilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

{1-[3-(2-metoxietilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

(1-{3-[(piridin-3-ilmetil)amino]-propil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

{1-[3-((S)-1-p-tolil-etilamino)propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

{1-[3-(4-metoxibencilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

{1-[3-(ciclopropilmetilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

{1-[3-(4-metilbencilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

(1-{2-[(1-hidroxi-ciclohexilmetil)-carbamoil]-1,1-dimetil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1,1-dimetil-2-[(tetrahidropiran-4-ilmetil)amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico

(1-{2-[(1-hidroxi-ciclohexilmetil)-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico

(1-{1-[(2,2,2-trifluoro-etilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

(1-{1-[(2,2-dimetilpropilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

(1-{1-[((R)-1-ciclohexil-etilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

[1-(1-dimetilaminometil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

[1-(1-piperidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

[1-(1-morfolin-4-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-[((2R,6S)-2,6-dimetil-morfolin-4-il)metil-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-[6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

(1-{2-[(4-hidroxi-tetrahidro-piran-4-ilmetil)-amino]-etil}-1H-imidazol- 4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico

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(1-{2-[(tetrahidro-piran-4-ilmetil)-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

(1-{2-[(3-metil-oxetan-3-ilmetil)-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

(1-{2-[(1-hidroxi-ciclohexilmetil)-amino]-1-metil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

(1-{1,1-dimetil-3-[(piridin-2-ilmetil)amino]-propil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico

(1-{1-[(1-hidroxi-ciclohexilmetil)-carbamoil]-1-metil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[2-((2R,6S)-2,6-dimetilmorfolin-4-il)-1,1-dimetiletil]-1H-imidazol-4-il}amida del ácido (S)-2-{[(2-fluoro-3-trifluorometil-fenil)metil]amino}-pentanoico

{1-[1,1-dimetil-3-((S)-2,2,2-trifluoro-1-fenil-etilamino)propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

{1-[1,1-dimetil-3-((R)-1-fenil-etilamino)propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico

{1-[2-((2R,6S)-2,6-dimetilmorfolin-4-il)-1,1-dimetiletil]-1H-imidazol-4-il}amida del ácido (S)-2-(2-trifluorometil-bencilamino)-pentanoico

(1-{1-metil-1-[(tetrahidro-piran-4-ilmetil)carbamoil]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

{1-[2-(2-etoxi-etilamino)-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8-

difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

{(R)-1-[(R)-1-(4-fluoro-fenil)-2-hidroxi-etil]-1H-imidazol-4-il}-amida del ácido (S)-2- [2-(3,5-difluoro-fenil)acetilamino]pentanoico

[1-(2-hidroximetil-fenil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico

{1-[2-(2-etoxi-etilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1-[2-(2-etoxi-etilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-propionamida

(S)-2-[2-(3,5-difluoro-fenil)acetilamino]-N-{1-[2-(2,2-dimetil-propilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-fenil-acetamida;

{1-[1-metil-1-(2-metil-bencilcarbamoil)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1-(2-metoxi-1-metil-etilcarbamoil)-1-metil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{(S)-1-[2-(2,2-dimetil-propilamino)-1-fenil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

[1-(3-bencilamino-propil)-1H-imidazol-4-il]amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

(1-{2-[(2,2-dimetil-propilamino)-metil]-fenil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{(S)-1-[2-(2,2-dimetil-propilamino)-1-fenil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{2-[(2-hidroxi-butilamino)-metil]-fenil}-1H-imidazol-4-il)amida del ácido (S)-2- (6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

2-[2-(3,5-difluoro-fenil)acetilamino]-N-{1-[2-(2,2-dimetil-propilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-piridin-3-il-acetamida;

2-[2-(3,5-difluoro-fenil)acetilamino]-N-{1-[2-(2,2-dimetil-propilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-(4-fluoro-fenil)-acetamida;

{1-[1-metil-1-(metilfenetil-carbamoil)-etil]-1H-imidazol-4-il}amida del ácido (S)- 2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1-(1,3-dihidro-isobenzofuran-5-ilcarbamoil)-1-metil-etil]-1H-imidazol-4- il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1-(indan-1-ilcarbamoil)-1-metil-etil]-1H-imidazol-4-il}amida del ácido (S)-2- (6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1,1-dimetil-2-oxo-2-(3-piridin-4-il-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-[2-(3-fluoro-fenil)-etilcarbamoil]-1-metiletil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)propionilamino]- imidazol-1-il}-N-indan-1-il-isobutiramida;

{1-[2-(3-ciano-piperidin-1-il)-1,1-dimetil-2-oxo-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-metil-1-[metil-(tetrahidro-piran-2-ilmetil)carbamoil]-etil}-1H-imidazol-4- il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

(1-{1-[etil-(2-pirazol-1-il-etil)carbamoil]-1-metiletil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1,1-dimetil-2-oxo-2-(2-fenil-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1-[1,1-dimetil-2-oxo-2-(3-piridin-4-il-pirrolidin-1-il)etil]-1H-imidazol-4-il}- propionamida;

(1-{1-[(furan-2-ilmetil)carbamoil]-1-metiletil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{2-[3-(acetil-metil-amino)pirrolidin-1-il]-1,1-dimetil-2-oxo-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1-metil-1-((3R,4S)-4-metilsulfanil-tetrahidro-furan-3-ilcarbamoil)etil]-1H- imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[2-(4-acetil-[1,4]diazepan-1-il)-1,1-dimetil-2-oxo-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino) propionilamino]-imidazol-1-il}-N-[2-(3-fluorofenil)-etil]-isobutiramida;

(1-{1-metil-1-[1-(1-metil-1H-pirazol-4-il)etilcarbamoil]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8 Difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino) propionilamino]-imidazol-1-il}-N-metil-N-fenetil-isobutiramida;

{1-[1-(3-metoxi-propilcarbamoil)-1-metiletil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-metil-1-[(3-metil-[1,2,4]oxadiazol-5-ilmetil)carbamoil]-etil}-1H-

imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-[(2-ciano-etil)-metilcarbamoil]-1-metil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino) propionilamino]-imidazol-1-il}-N-etil-N-(2-pirazol-1-il-etil)-isobutiramida;

{1-[1,1-dimetil-2-(3-metil-5,6-dihidro-8H-[1,2,4]triazolo[4,3-a]pirazin-7-il)-2-oxo-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-metil-1-[metil-(1-metil-1H-imidazol-2-ilmetil)carbamoil]-etil}-1H-imidazol-4- il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1-[2-(4-hidroximetil-4-metilpiperidin-1-il)-1,1-dimetil-2-oxo-etil]-1H-imidazol-4-il} propionamida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)propionilamino]- imidazol-1-il}-N-(4-metil-bencil)-isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-(1,3-dihidro-isobenzofuran-5-il)-isobutiramida;

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1-[1,1-dimetil-2-oxo-2-(2-fenilpirrolidin-1-il)-etil]-1H-imidazol-4-il}-propionamida;

(1-{1-[(2-dietilamino-etil)metil-carbamoil]-1-metil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(S)-N-{1-[2-(3-ciano-piperidin-1-il)-1,1-dimetil-2-oxo-etil]-1H-imidazol-4-il}-

2- (6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionamida;

(S)-N-(1-{2-[3-(acetil-metil-amino)-pirrolidin-1-il]-1,1-dimetil-2-oxo-etil}-1H-imidazol-4-il)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionamida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-((1R,2S)-2-hidroximetil-ciclohexil)isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-(3-metil-[1,2,4]oxadiazol-5-ilmetil)isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]- imidazol-1-il}-N-((S)-2-metoxi-1-metil-etil)isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]- imidazol-1-il}-N-(3-metoxipropil)isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]- imidazol-1-il}-N-[1-(1-metil-1H-pirazol-4-il)-etil]-isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]- imidazol-1-il}-N-(3-imidazol-1-il-propil)-isobutiramida; y

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]- imidazol-1-il}-N-(3-morfolin-4-il-propil)-isobutiramida;

La invención descrita y reivindicada en esta memoria descriptiva no está limitada en alcance por las realizaciones específicas descritas en esta memoria descriptiva, ya que estas realizaciones se pretenden como ilustraciones de varios aspectos de la invención. Cualesquiera realizaciones equivalentes se pretende que estén incluidas dentro del alcance de esta invención. De hecho, diversas modificaciones de la invención además de las mostradas y descritas

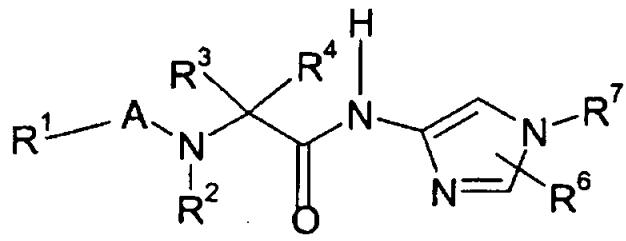
en esta memoria descriptiva se harán evidentes para los expertos en la técnica a partir de la descripción anterior. Tales modificaciones se pretende también que caigan dentro del alcance de las reivindicaciones anexas.

Habiendo descrito la invención como antecede se declara como propiedad lo contenido en las siguientes

REIVINDICACIONES

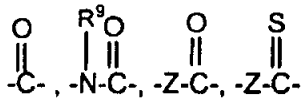
Lo que se reivindica es lo siguiente:

1. Un compuesto de fórmula I



I

en la que A está ausente o se selecciona entre



Z se selecciona entre $-CH_2$, -CH(OH), -CH(alquilo C_1 - C_6), -CH(alcoxi C_1 - C_6), $-CH(NR^9R^{10})$, $-CH(CH_2(OH))$, -CH(CH(alquilo C_1 - C_4)(OH)) y -CH(C(alquilo C_1 - C_4)(alquilo C_1 - C_4)(OH));

R^1 se selecciona entre alquilo C_1 - C_{20}, alquenilo C_2 - C_{20}, alquinilo C_2 - C_{20}, alcoxi C_1 - C_{20}, alquenoxi C_2 - C_{20}, hidroxialquilo C_1 - C_{20}, cicloalquilo C_3 - C_8, benzo (cicloalquilo C_3 - C_8), benzo (heterocicloalquilo C_3 - C_8), cicloalquenilo C_4 - C_8, bi- o tricicloalquilo (C_5 - C_{11}), benzo bi- o tricicloalquilo (C_5 - C_{11}), bi- o

tricicloalquenilo (C_7 - C_{11}), heterocicloalquilo de (entre 3 y 8 miembros), arilo C_6 - C_{14} y heteroarilo de (entre 5 y 14 miembros), en el que R^1 está opcionalmente sustituido con R^{1a};

en la que R^{1a} en cada caso se selecciona independientemente entre - OH, halo, -alcoxi C_1 - C_6, -CN, -NO_2, NR^9R^{10}, -C(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, - SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), - heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

en la que dicho alcoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{1a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{1b};

en la que R^{1b} se selecciona en cada caso independientemente entre - OH, - alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, - alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -NR^9R^{10}, -C-(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

R^2 se selecciona entre H, alquilo C_1 - C_6, alquenilo C_2 - C_6, cicloalquilo C_3 - C_8 y cicloalquenilo C_3 - C_8, en el que R^2 está sustituido opcional e independientemente con entre uno a tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_4 opcionalmente sustituido con entre

uno a tres átomos halo, alcoxi C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, halo y -OH.

o R^1 y R^2 junto con el grupo A cuando está presente y el átomo de nitrógeno al que R^2 está unido, o R^1 y R^2 junto con el átomo de nitrógeno al que R^1 y R^2 están unidos cuando A está ausente, pueden opcionalmente formar un anillo de cuatro a ocho miembros;

R^3 se selecciona entre H, alquilo C_1 - C_6, alquenilo C_2 - C_6, alquinilo C_2 - C_6, cicloalquilo C_3 - C_6, cicloalquenilo C_5 - C_6 y heterocicloalquilo de (entre 3 y 8 miembros), -arilo C_6 - C_{14} y heteroarilo de (entre 5 y 14 miembros), en el que dicho alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquenilo, heterocicloalquilo, arilo o heteroarilo están cada uno de ellos opcional e independientemente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre alcoxi C_1 - C_4, halo, -OH, -S alquilo (C_1 - C_4), -alquilo (C_1 - C_4), $-C(=O)OR^9$, $-SO_2R^9$ y heterocicloalquilo de (entre 3 y 8 miembros) en el que dicho alquilo, alcoxi, y heterocicloalquilo puede estar adicionalmente sustituido con uno a seis halo;

R^4 es H, alquilo C_1 - C_6 o halo;

o R^3 y R^4 pueden junto con el átomo de carbono al que están unidos opcionalmente formar un resto seleccionado entre ciclopropilo, ciclobutilo, ciclopentilo, ciclohexilo, morfolino, piperidino, pirrolidino, tetrahidrofuranilo y perhidro-2H-pirano, en el que dicho resto formado por R^3 y R^4 está opcionalmente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, alcoxi C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, halo, -OH, -CN y alilo;

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R^6 se selecciona entre H, alquilo C_1 - C_6, alquileno C_2 - C_6, alcoxi C_1 - C_6, halo, -CN, cicloalquilo C_3 - C_{12}, cicloalquenilo C_4 - C_{12}, heteroarilo de (entre 5 y 10 miembros) y arilo C_6 - C_{10}, en el que dicho alquilo, alquileno y alcoxi de R^6 están cada uno de ellos opcional e independientemente sustituidos con entre uno a tres sustituyentes seleccionados independientemente entre halo y -CN, y en el que dicho cicloalquilo, cicloalquenilo, heteroarilo y arilo de R^6 están cada uno de ellos opcional e independientemente sustituidos con entre uno a tres sustituyentes seleccionados independientemente entre -alquilo C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, halo y -CN;

R^7 es alquilo C_1 - C_{20} sustituido con -cicloalquilo C_3 - C_{12}, cicloalquenilo C_4 - C_{12}, bi- o tricicloalquilo (C_5 - C_{20}), bi- o tricicloalquenilo (C_7 - C_{20}), heterocicloalquilo de (entre 3 y 12 miembros), heterobi- o heterotricicloalquilo de (entre 7 y 20 miembros), arilo C_6 - C_{14}, benzo (heterocicloalquilo C_3 - C_8), heteroarilo de (entre 5 y 15 miembros), -ariloxi C_6 - C_{15} y -heteroariloxi de (entre 5 y 15 miembros), en el que R^7 está independientemente sustituido con entre uno y seis sustituyentes seleccionados independientemente entre R^{7a};

o R^7 es -cicloalquilo C_3 - C_{20}, -cicloalquenilo C_4 - C_{12}, bi- o tricicloalquilo (C_5 - C_{20}), bi- o tricicloalquenilo (C_7 - C_{20}), -heterocicloalquilo de (entre 3 y 12 miembros), -heterobi o heterotricicloalquilo de (entre 7 y 20 miembros) , -arilo C_6 - C_{14}, benzo (cicloalquilo C_3 - C_8), heteroarilo de (entre 5 y 15 miembros), -ariloxi C_6 - C_{15} y -heteroariloxi de (entre 5 y 15 miembros) sustituido con al menos un -alquilo C_1 - C_{20}, en el que dichos cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, heterobi o heterotricicloalquilo, arilo, benzocicloalquilo, heteroarilo, ariloxi y heteroariloxi

está opcional e independientemente sustituido con entre uno y seis sustituyentes seleccionados independientemente entre R^{7a}; en el que dicho alquilo está sustituido con R^{7C};

en la que R^{7a} en cada caso se selecciona independientemente entre -OH, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alquilo, alquenilo, alquinilo, alcoxi, alquenoxi, alquinoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{7a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{7b};

en la que R^{7b} en cada caso se selecciona independientemente entre -OH, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

en la que R^{7C} en cada caso se selecciona independientemente entre -

alcoxi C_1 - C_6, -CN, -NO_2, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alquenoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{7c} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{7b};

o R^6 y R^7 pueden junto con los átomos de carbono y nitrógeno a los que están respectivamente unidos opcionalmente formar un anillo heterocicloalquilo de (entre 5 y 8 miembros), un anillo heterocicloalquenilo de (entre 5 y 8 miembros) o un anillo heteroarilo de (entre 6 y 8 miembros) , en el que dichos anillos heterocicloalquilo, heterocicloalquenilo y heteroarilo están opcional e independientemente sustituidos cada uno con entre uno a tres sustituyentes seleccionados independientemente entre halo, -alquilo C_1 - C_6, opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, -hidroxialquilo C_1 - C_6, -OH, -$(CH_2)_{cero\text{ - }10}$ NR^9R^{10}, -$(CH_2)_{cero\text{ - }10}$ $C(=O)NR^9R^{10}$, -$SO_2NR^9R^{10}$ y -cicloalquilo C_3 - C_{12};

R^9 y R^{10} en cada caso se seleccionan cada uno de ellos independientemente entre H, -OH, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o

tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alquilo, alquenilo, alquinilo, alcoxi, alquenoxi, alquinoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^9 y R^{10} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{10a};

en la que R^{10a} en cada caso se selecciona independientemente entre -OH, halo, -hidroxialquilo C_1 - C_{12}, -alcoxi C_1 - C_6, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, -cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alcoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{10a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{10b};

en la que R^{10b} en cada caso se selecciona independientemente entre -OH, halo, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de

4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

o NR^9R^{10} puede formar un heterocicloalquilo de (entre 4 y 20 miembros), heterobi- o tricicloalquilo de (entre 5 y 18 miembros), heterobi- o tricicloalquenilo de (entre 5 y 18 miembros), o heteroarilo de (entre 5 y 15 miembros), en el que dicho heterocicloalquilo, heterobi- o tricicloalquilo, heterobi- o tricicloalquenilo o heteroarilo están opcionalmente e independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre alquilo C_1 - C_6, -alquenilo C_2 - C_6, -alquenilo C_2 - C_6, alcoxi C_1 - C_6, alquenoxi C_2 - C_6, alquinoxi C_2 - C_6, hidroxialquilo C_1 - C_6, hidroxialquenilo C_2 - C_6, -hidroxialquenilo C_2 - C_6, halo, -OH, -CN, $-NO_2$, $-NR^{11}R^{12}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-S(O)_nR^{11}$ y $-S(O)_nNR^{11}R^{12}$;

R^{11} y R^{12} en cada caso se seleccionan independientemente cada uno entre H, alquilo C_1 - C_8, cicloalquilo C_3 - C_8, cicloalquenilo C_4 - C_8, bi- o tricicloalquilo (C_5 - C_{11}), bi- o tricicloalquenilo (C_7 - C_{11}), heterocicloalquilo de (entre 3 y 8 miembros), arilo C_6 - C_{10} y heteroarilo de (entre 5 y 14 miembros), en el que dicho alquilo de R^{11} está opcional e independientemente sustituido con entre uno y tres sustituyentes seleccionados independientemente entre -OH, - CN y cicloalquilo C_3 - C_8, y en el que cada átomo de hidrógeno de dicho alquilo está opcional e independientemente reemplazado con un átomo halo, y en el que dicho cicloalquilo, cicloalquenilo, heterocicloalquilo, arilo y heteroarilo de R^{11} están cada uno de ellos opcional e independientemente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre halo, alquilo C_1 - C_8 opcionalmente sustituido con entre uno a tres átomos halo, -OH,

-CN y cicloalquilo C_3 - C_8; y

n es en cada caso un número entero seleccionado independientemente entre cero, 1 y 2;

o una sal farmacéuticamente aceptable del mismo.

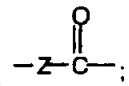
2. El compuesto de la reivindicación 1, en el que R^7 es un -cicloalquilo C_4 - C_8, -heterocicloalquilo de (entre 4 y 10 miembros), -arilo C_6 - C_{14}, o -heteroarilo de (entre 5 y 15 miembros), sustituido con un -alquilo C_1 - C_4 y en el que dicho alquilo está sustituido adicionalmente con R^{7C}, en el que R^{7C} es -NR^9R^{10}.

3. El compuesto de la reivindicación 2, en el que R^9 es hidrógeno o metilo, R^{10} es -alquilo C_1 - C_8, o -cicloalquilo C_4 - C_8, en el que dicho alquilo o cicloalquilo de R^{10} está opcionalmente sustituido con entre uno a seis sustituyentes seleccionados entre R^{10a} en el que R^{10a} se selecciona entre halo, -alquilo C_1 – C_4, -cicloalquilo C_4 - C_8, -heteroarilo de (entre 5 y 15 miembros), o -hidroxialquilo C_1 - C_4; o -NR^9R^{10} es un heterocicloalquilo de (entre 4 y 6 miembros) opcionalmente sustituido con entre uno y seis sustituyentes seleccionados entre halo, -alquilo C_1 - C_4 o -hidroxialquilo C_1 - C_4.

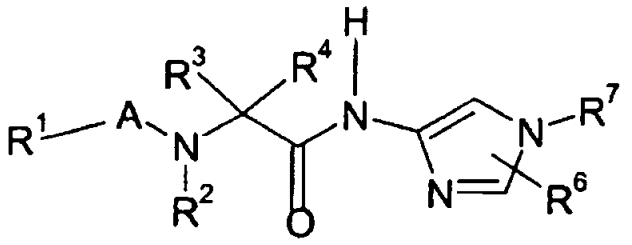
4. El compuesto de la reivindicación 1, en el que R^7 es un -alquilo C_1 - C_8 sustituido con un -cicloalquilo C_4 - C_8; -bi- o tricicloalquilo (C_5 - C_{20}), heterocicloalquilo de (entre 4 y 8 miembros), -heterobi- o heterotricicloalquilo de (entre 7 y 12 miembros), -arilo C_6 - C_{14}, -benzo(cicloalquilo C_3 - C_8), -heteroarilo de entre (5 y 15 miembros), en el que R^7 está opcionalmente

independientemente sustituido con entre uno y seis sustituyentes seleccionados independientemente entre R^{7a}, en el que R^{7a} es $-NR^9R^{10}$, halo, -alquilo C_1 - C_4 o -hidroxialquilo C_1 - C_4.

5. El compuesto de la reivindicación 4, en el que R^7 es un -alquilo C_1 - C_6 sustituido con heterocicloalquilo de (entre 4 y 8 miembros) o -arilo C_6 - C_{14}, en el que R^7 está opcionalmente independientemente sustituido con entre uno y seis sustituyentes seleccionados independientemente entre R^{7a}, en el que R^{7a} es $-NR^9R^{10}$, halo, -OH, -alquilo C_1 - C_4 o -hidroxialquilo C_1 - C_4, en el que dicho alquilo o hidroxialquilo está opcionalmente sustituido con entre uno y seis halo.

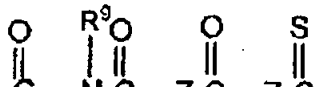
6. El compuesto de la reivindicación 1, en el que A está ausente y R^1 es benzo (cicloalquilo C_5 - C_6) opcionalmente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_6, halo y OH; o A es  ; Z es $-CH_2$, -CH(OH) o -CH(alquilo C_1 - C_6) y R^1 es alquilo C_1 - C_{10}, arilo C_6 - C_{10}, o heteroarilo de (entre 6 y 10 miembros), en el que dicho alquilo, arilo y heteroarilo están opcionalmente independientemente sustituidos con entre uno y tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_6, halo, y OH; R^2 es H o alquilo C_1 - C_6; R^3 es H, $-CH_2CH_2SCH_3$, $-CH_2CH_2OCH_3$, o alquilo C_1 - C_6; R^4 es H y R^6 es H o alquilo C_1 - C_6.

7. Un compuesto de fórmula I



I

en la que A está ausente o se selecciona entre



Z se selecciona entre -CH_2, -CH(OH), -CH(alquilo C_1 - C_6), -CH(alcoxi C_1 - C_6), -$CH(NR^9R^{10})$, -$CH(CH_2(OH))$, -CH(CH(alquilo C_1 - C_4)(OH)) y -CH(C(alquil C_1 - C_4) (alquilo C_1 - C_4)(OH));

R^1 se selecciona entre -alquilo C_1 - C_{20}, -alquenilo C_2 - C_{20}, alquinilo C_2 - C_{20}, -alcoxi C_1 - C_{20}, -alquenoxi C_2 - C_{20}, -hidroxialquilo C_1 - C_{20}, -cicloalquilo C_3 - C_8, benzo(cicloalquilo C_3 - C_8), benzo(heterocicloalquilo C_3 - C_8), -cicloalquenilo C_4 - C_8, -bi- o tricicloalquilo (C_5 - C_{11}), benzo bi o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 3 a 8 miembros), -arilo C_6 - C_{14} y -heteroarilo (de 5 a 14 miembros), en el que R^1 está opcionalmente sustituido con R^{1a};

en el que R^{1a} se selecciona en cada caso independientemente entre -OH, halo, -alcoxi C_1 - C_6, -CN, -NO_2, -NR^9R^{10}, -C- (=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15

miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

en la que dicho alcoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{1a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{1b};

en la que R^{1b} se selecciona en cada caso independientemente entre -OH, - alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -NR^9R^{10}, -C-(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

R^2 se selecciona entre H, -alquilo C_1 - C_6, -alquenilo C_2 - C_6, -cicloalquilo C_3 - C_8 y -cicloalquenilo C_3 - C_8, en el que R^2 está opcional e independientemente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, alcoxi C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, halo y –OH;

o R^1 y R^2 junto con el grupo A cuando está presente y el átomo de nitrógeno al que R^2 está unido, o R^1 y R^2 junto con el átomo de nitrógeno al que R^1 y R^2 están unidos cuando A está ausente, pueden opcionalmente formar un anillo de cuatro a ocho miembros;

R^3 se selecciona entre H, -alquilo C_1 - C_6, -alquenilo C_2 - C_6, -alquinilo C_2 - C_6, -cicloalquilo C_3 - C_6, -cicloalquenilo C_5 - C_6 y heterocicloalquilo de (entre 3

y 8 miembros), -arilo C_6 - C_{14} y heteroarilo de (entre 5 y 14 miembros), en el que dicho alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquenilo, heterocicloalquilo, arilo o heteroarilo están cada uno de ellos opcional e independientemente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre -alcoxi C_1 - C_4, halo, -OH, -S alquilo (C_1 - C_4), -alquilo (C_1 - C_4), $-C(=O)OR^9$, $-SO_2R^9$ y heterocicloalquilo de (entre 3 y 8 miembros) en el que dicho alquilo, alcoxi, y heterocicloalquilo puede estar adicionalmente sustituido con uno a seis halo;

R^4 es H, alquilo C_1 - C_6 o halo;

o R^3 y R^4 pueden junto con el átomo de carbono al que están unidos opcionalmente formar un resto seleccionado entre ciclopropilo, ciclobutilo, ciclopentilo, ciclohexilo, morfolino, piperidino, pirrolidino, tetrahidrofuranilo y perhidro-2H-pirano, en el que dicho resto formado por R^3 y R^4 está opcionalmente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, alcoxi C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, halo, -OH, -CN y alilo;

R^6 se selecciona entre H, -alquilo C_1 - C_6, -alquileno C_2 - C_6, -alcoxi C_1 - C_6, halo, -CN, cicloalquilo C_3 - C_{12}, cicloalquenilo C_4 - C_{12}; heteroarilo de (entre 5 y 10 miembros) y -arilo C_6 - C_{10}, en el que dicho alquilo, alquileno y alcoxi de R^6 están cada uno de ellos opcional e independientemente sustituidos con entre uno a tres sustituyentes seleccionados independientemente entre halo y -CN, y en el que dicho cicloalquilo, cicloalquenilo, heteroarilo y arilo de R^6 están cada uno de ellos opcional e independientemente sustituidos con entre uno a tres sustituyentes seleccionados independientemente entre -alquilo C_1 - C_4

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opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, halo y -CN;

R^7 se selecciona entre -alquilo C_1 - C_{20}, -alcoxi C_1 - C_{20}, -hidroxialquilo C_1 - C_{20}, -cicloalquilo C_3 - C_{12}, cicloalquenilo C_4 - C_{12}, bi- o tricicloalquilo (C_5 - C_{20}), bi- o tricicloalquenilo (C_7 - C_{20}), heterocicloalquilo de (entre 3 y 12 miembros), heterobi- o heterotricicloalquilo de (entre 7 y 20 miembros), arilo C_6 - C_{14}, heteroarilo de (entre 5 y 15 miembros), -ariloxi C_6 - C_{15} y -heteroariloxi de (entre 5 y 15 miembros), en el que dichos alquilo, alquenilo, alquinilo, alcoxi, alquenoxi, alquinoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^7 están cada uno de ellos independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo de R^{7a} o están cada uno de ellos opcional e independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo de R^{7d};

en la que R^{7a} en cada caso se selecciona independientemente entre -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -cicloalquilo C_3 - C_{15}, -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alquilo, alcoxi, alcoxialquilo, cicloalquilo, heterocicloalquilo, arilo, heteroarilo, ariloxi, y heteroariloxi de R^{7a} están cada uno independientemente sustituidos con R^{7b};

en la que R^{7d} en cada caso se selecciona independientemente entre -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -SO_2-NR^9R^{10}, -cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), en el que

dicho alquenilo, alquinilo, hidroxialquilo, alquenoxi, alquinoxi, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, de R^{7d} están cada uno de ellos opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{7b};

en la que R^{7b} en cada caso se selecciona independientemente entre -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2- NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

o R^6 y R^7 pueden junto con los átomos de carbono y nitrógeno a los que están respectivamente unidos opcionalmente formar un anillo heterocicloalquilo de (entre 5 y 8 miembros), un anillo heterocicloalquenilo de (entre 5 y 8 miembros) o un anillo heteroarilo de (entre 6 y 8 miembros) , en el que dichos anillos heterocicloalquilo, heterocicloalquenilo y heteroarilo están opcional e independientemente sustituidos cada uno con entre uno a tres sustituyentes seleccionados independientemente entre halo, -alquilo C_1 - C_6, opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, -hidroxialquilo C_1 - C_6, -OH, -$(CH_2)_{cero\ -\ 10}$ NR^9R^{10}, -$(CH_2)_{cero\ -\ 10}$ $C(=O)NR^9R^{10}$, -$SO_2NR^9R^{10}$ y cicloalquilo C_3 - C_{12};

R^9 y R^{10} se seleccionan en cada caso cada uno de ellos independientemente entre H, -$C(=O)R^{13}$ o -alquilo C_1 - C_{20}, en el que al menos

uno de R^9 y R^{10} son -C(=O)R^{13} o -alquilo C_1 - C_{20}, y en el que cada -alquilo C_1 - C_{20}, está sustituido con R^{10a};

en la que R^{10a} en cada caso se seleccionan independientemente entre -alcoxi C_1 - C_6, -CN, -NO_2, -$NR^{11}R^{11}$, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{11}, -SO_2-$NR^{11}R^{12}$, -S(O)$_n$-R^{11}, -cicloalquilo C_3 - C_{15}, -cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho, alcoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{10a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{10b};

en la que R^{10b} en cada caso se selecciona independientemente entre -OH, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -$NR^{11}R^{12}$, -C(=O)$NR^{11}R^{12}$, -C(=O)R^{11}, -C(=O)OR^{11}, -SO_2-$NR^{11}R^{12}$, -S(O)$_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

o NR^9R^{10} puede formar un heterocicloalquilo de (entre 4 y 20 miembros), heterobi- o tricicloalquilo de (entre 5 y 18 miembros), heterobi- o tricicloalquenilo de (entre 5 y 18 miembros), o heteroarilo de (entre 5 y 15 miembros), en el que dicho heterocicloalquilo, heterobi- o tricicloalquilo, heterobi- o tricicloalquenilo o heteroarilo están opcionalmente e

independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre -alquilo C_1 - C_6, -alquenilo C_2 - C_6, - alquenilo C_2 - C_6, - alcoxi C_1 - C_6, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, - hidroxialquilo C_1 - C_6, - hidroxialquenilo C_2 - C_6, - hidroxialquenilo C_2 - C_6, halo, -OH, -CN, $-NO_2$, $-NR^{11}R^{12}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)R^{11}$, $-C(=O)OR^{11}$, $-S(O)_nR^{11}$ y $-S(O)_nNR^{11}R^{12}$;

en el que R^{11} y R^{12} en cada caso se seleccionan independientemente cada uno entre H, -alquilo C_1 - C_8, -cicloalquilo C_3 - C_8, -cicloalquenilo C_4 - C_8, bi- o tricicloalquilo (C_5 - C_{11}), bi- o tricicloalquenilo (C_7 - C_{11}), heterocicloalquilo de (entre 3 y 8 miembros), -arilo C_6 - C_{10} y -heteroarilo de (entre 5 y 14 miembros), en el que dicho alquilo de R^{11} y R^{12} está opcional e independientemente sustituido con entre uno y tres sustituyentes seleccionados independientemente entre - OH, - CN y cicloalquilo C_3 - C_8, y en el que cada átomo de hidrógeno de dicho alquilo está opcional e independientemente reemplazado con un átomo halo, y en el que dicho cicloalquilo, cicloalquenilo, heterocicloalquilo, arilo y heteroarilo de R^{11} están cada uno de ellos opcional e independientemente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre halo, alquilo C_1 - C_8 opcionalmente sustituido con entre uno a tres átomos halo, -OH, -CN y cicloalquilo C_3 - C_8;

R^{13} en cada caso se selecciona independientemente entre alquilo sustituido con -alcoxi C_1 - C_{12}, cicloalquilo C_3 – C_{15}, cicloalquenilo C_4 - C_{15}, bi- o tricicloalquilo (C_5 - C_{11}), bi- o tricicloalquenilo (C_7 - C_{11}), heterocicloalquilo de (entre 4 y 20 miembros), arilo C_6 - C_{15}, heteroarilo de (entre 5 y 15 miembros), - ariloxi C_6 - C_{15} y heteroariloxi de (entre 5 y 15 miembros); en el que dicho alcoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo,

heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{13} está opcionalmente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre halo, -alquilo C_1 - C_8 opcionalmente sustituido con entre uno a tres átomos halo, -OH, -CN y cicloalquilo C_3 - C_8; y

n es en cada caso un número entero seleccionado independientemente entre cero, 1 y 2;

o una sal farmacéuticamente aceptable del mismo.

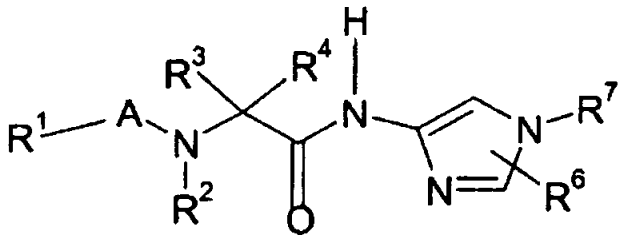
8. El compuesto de la reivindicación 7, en el que R^7 es un -alquilo C_1 - C_8 sustituido con R^{7a}; R^{7a} es $-NR^9R^{10}$; R^9 es H o metilo; R^{10} es un alquilo C_1 - C_8; R^{10a} es alcoxi C_1 - C_6, -cicloalquilo C_4 - C_8, -heterocicloalquilo de (entre 4 y 8 miembros), arilo C_6 - C_{15} o heteroarilo de (entre 5 y 15 miembros), en el que dicho alcoxi, cicloalquilo, heterocicloalquilo, arilo, heteroarilo de R^{10a} están cada uno de ellos opcional e independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo de R^{10b}; en el que R^{10b} es halo, -OH, -alquilo C_1 - C_4 o -hidroxialquilo C_1 - C_4, en el que dicho alquilo o hidroxialquilo de R^{10b} está opcionalmente sustituido con uno a seis halo.

9. El compuesto de la reivindicación 7, en el que R^7 es un -alquilo C_1 - C_8 sustituido con R^{7a}; R^{7a} es $-C(=O)NR^9R^{10}$; R^9 es H o metilo; R^{10} es un alquilo C_1 - C_8; R^{10a} es alcoxi C_1 - C_6, -cicloalquilo C_4 - C_8, -heterocicloalquilo de (entre 4 y 8 miembros), arilo C_6 - C_{15} o heteroarilo de (entre 5 y 15 miembros), en el que dicho alcoxi, cicloalquilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{10a} están cada uno de ellos opcional e independientemente

sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo de R^{10b}; en el que R^{10b} es halo, -OH, -alquilo C_1 - C_4 o -hidroxialquilo C_1 - C_4, en el que dicho alquilo o hidroxialquilo de R^{10b} está opcionalmente sustituido con uno a seis halo.

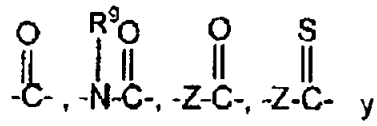
10. El compuesto de la reivindicación 7, en el que A está ausente y R^1 es -benzo (cicloalquilo C_5 - C_6) opcionalmente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_6, halo y OH; o A es  ; Z es $-CH_2$, -CH(OH) o -CH(alquilo C_1 - C_6) y R^1 es alquilo C_1 - C_{10}, arilo C_6 - C_{10}, o heteroarilo de (entre 6 y 10 miembros), en el que dicho alquilo, arilo y heteroarilo están opcionalmente sustituidos independientemente con entre uno y tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_6, halo, y OH; R^2 es H o alquilo C_1 - C_6; R^3 es H, $-CH_2CH_2SCH_3$, $-CH_2CH_2OCH_3$, o alquilo C_1 - C_6; R^4 es H y R^6 es H o alquilo C_1 - C_6.

11. Un compuesto de fórmula I



I

en la que A está ausente o se selecciona entre



Z se selecciona entre $-CH_2$, -CH(OH), -CH(alquilo C_1 - C_6), -CH(alcoxi C_1 - C_6), $-CH(NR^9R^{10})$, $-CH(CH_2(OH))$, $-CH(CH(\text{alquilo } C_1 - C_4)(OH))$ y $-CH(C(\text{alquil } C_1 - C_4)(\text{alquilo } C_1 - C_4)(OH))$;

R^1 se selecciona entre -alquilo C_1 - C_{20}, -alquenilo C_2 - C_{20}, alquinilo C_2 - C_{20}, -alcoxi C_1 - C_{20}, -alquenoxi C_2 - C_{20}, -hidroxialquilo C_1 - C_{20}, -cicloalquilo C_3 - C_8, benzo(cicloalquilo C_3 - C_8), benzo(heterocicloalquilo C_3 - C_8), -cicloalquenilo C_4 - C_8, -bi- o tricicloalquilo (C_5 - C_{11}), benzo bi o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 3 a 8 miembros), -arilo C_6 - C_{14} y -heteroarilo (de 5 a 14 miembros), en el que R^1 está opcionalmente sustituido con R^{1a};

en el que R^{1a} se selecciona en cada caso independientemente entre -OH, halo, -alcoxi C_1 - C_6, -CN, $-NO_2$, $-NR^9R^{10}$, -C- $(=O)NR^9R^{10}$, $-C(=O)R^{11}$, $-C(=O)OR^{12}$, $-SO_2-NR^9R^{10}$, $-S(O)_n-R^{11}$, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

en la que dicho alcoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{1a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{1b};

en la que R^{1b} se selecciona en cada caso independientemente entre -

OH, - alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, - alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -NR^9R^{10}, -C-(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

R^2 se selecciona entre H, -alquilo C_1 - C_6, -alquenilo C_2 - C_6, -cicloalquilo C_3 - C_8 y -cicloalquenilo C_3 - C_8, en el que R^2 está sustituido opcional e independientemente con entre uno a tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, alcoxi C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, halo y –OH;

o R^1 y R^2 junto con el grupo A cuando está presente y el átomo de nitrógeno al que R^2 está unido, o R^1 y R^2 junto con el átomo de nitrógeno al que R^1 y R^2 están unidos cuando A está ausente, pueden opcionalmente formar un anillo de cuatro a ocho miembros;

R^3 se selecciona entre -arilo C_6 - C_{14}, y heteroarilo de (entre 5 y 14 miembros), en el que dicho arilo o heteroarilo están cada uno de ellos opcional e independientemente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre -alcoxi C_1 - C_4, halo, -OH, -S alquilo (C_1 - C_4), -alquilo (C_1 - C_4), -C(=O)OR^9, -SO_2R^9 y heterocicloalquilo de (entre 3 y 8 miembros) en el que dicho alquilo, alcoxi, y heterocicloalquilo puede estar adicionalmente sustituido con uno a seis halo;

R^4 es H, alquilo C_1 - C_6 o halo;

o R^3 y R^4 pueden junto con el átomo de carbono al que están unidos opcionalmente formar un resto seleccionado entre ciclopropilo, ciclobutilo, ciclopentilo, ciclohexilo, morfolino, piperidino, pirrolidino, tetrahidrofuranilo y perhidro-2H-pirano, en el que dicho resto formado por R^3 y R^4 está opcionalmente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre -alquilo C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, halo, -OH, -CN y alilo;

R^6 se selecciona entre H, -alquilo C_1 - C_6, -alquileno C_2 - C_6, -alcoxi C_1 - C_6, halo, -CN, cicloalquilo C_3 - C_{12}, cicloalquenilo C_4 - C_{12}, heteroarilo de (entre 5 y 10 miembros) y -arilo C_6 - C_{10}, en el que dicho alquilo, alquileno y alcoxi de R^6 están cada uno de ellos opcional e independientemente sustituidos con entre uno a tres sustituyentes seleccionados independientemente entre halo y -CN, y en el que dicho cicloalquilo, cicloalquenilo, heteroarilo y arilo de R^6 están cada uno de ellos opcional e independientemente sustituidos con entre uno a tres sustituyentes seleccionados independientemente entre -alquilo C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, halo y -CN;

R^7 se selecciona entre H, -alquilo C_1 - C_{20}, -alcoxi C_1 - C_{20}, -hidroxialquilo C_1 - C_{20}, -cicloalquilo C_3 - C_{12}, cicloalquenilo C_4 - C_{12}, -bi- o tricicloalquilo (C_5 - C_{20}), -bi- o tricicloalquenilo (C_7 - C_{20}), heterocicloalquilo de (entre 3 y 12 miembros), -heterobi- o heterotricicloalquilo de (entre 7 y 20 miembros), arilo C_6 - C_{14}, y heteroarilo de (entre 5 y 15 miembros), en el que dichos alquilo, alquenilo, alquinilo, alcoxi, alquenoxi, alquinoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y

heteroariloxi de R^7 están cada uno de ellos opcional e independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo de R^{7a};

en la que R^{7a} en cada caso se selecciona independientemente entre -OH, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, - alcoxi C_1 - C_6, - alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alquilo, alquenilo, alquinilo, alcoxi, alquenoxi, alquinoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi, y heteroariloxi de R^{7a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo de R^{7b};

en la que R^{7b} en cada caso se selecciona independientemente entre -OH, -alquilo C_1 - C_{12}, alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, - alcoxialquilo C_1 - C_{12}, - hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, - NR^9R^{10}, -$C(=O)NR^9R^{10}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

o R^6 y R^7 pueden junto con los átomos de carbono y nitrógeno a los que

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están respectivamente unidos opcionalmente formar un anillo heterocicloalquilo de (entre 5 y 8 miembros), un anillo heterocicloalquenilo de (entre 5 y 8 miembros) o un anillo heteroarilo de (entre 6 y 8 miembros) , en el que dichos anillos heterocicloalquilo, heterocicloalquenilo y heteroarilo están opcional e independientemente sustituidos cada uno con entre uno a tres sustituyentes seleccionados independientemente entre halo, -alquilo C_1 - C_6, opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, -hidroxialquilo C_1 - C_6, -OH, -$(CH_2)_{cero\text{ - }10}$ NR^9R^{10}, -$(CH_2)_{cero\text{ - }10}$ $C(=O)NR^9R^{10}$, -$SO_2NR^9R^{10}$ y cicloalquilo C_3 - C_{12};

R^9 y R^{10} en cada caso se seleccionan cada uno de ellos independientemente entre H, -OH, alquilo C_1 - C_{12}, alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, - hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2- $NR^{10}R^{11}$, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), -ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros), en el que dicho alquilo, alquenilo, alquinilo, alcoxi, alquenoxi, alquinoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^9 y R^{10} están cada uno de ellos sustituidos opcional e independientemente con entre uno y seis sustituyentes seleccionados independientemente entre el grupo de R^{10a};

en la que R^{10a} en cada caso se selecciona independientemente entre - OH, halo, - alcoxi C_1 - C_6, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -

$C(=O)OR^{12}$, $-SO_2-NR^{11}R^{12}$, $-S(O)_n-R^{11}$, -cicloalquilo C_3 - C_{15}, -cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alcoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{10a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{10b};

en la que R^{10b} en cada caso se selecciona independientemente entre -OH, halo, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, $-NO_2$, $-NR^{11}R^{12}$, $-C(=O)NR^{11}R^{12}$, $-C(=O)R^{11}$, $-C(=O)OR^{12}$, $-SO_2-NR^{11}R^{12}$, $-S(O)_n-R^{11}$, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

o NR^9R^{10} puede formar un heterocicloalquilo de (entre 4 y 20 miembros), heterobi- o tricicloalquilo de (entre 5 y 18 miembros), heterobi- o tricicloalquenilo de (entre 5 y 18 miembros), o heteroarilo de (entre 5 y 15 miembros), en el que dicho heterocicloalquilo, heterobi- o tricicloalquilo, heterobi- o tricicloalquenilo o heteroarilo están opcionalmente e independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre -alquilo C_1 - C_6, -alquenilo C_2 - C_6, - alquenilo C_2 - C_6, - alcoxi C_1 - C_6, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, - hidroxialquilo C_1 - C_6, - hidroxialquenilo C_2 - C_6, - hidroxialquenilo C_2 - C_6, halo,

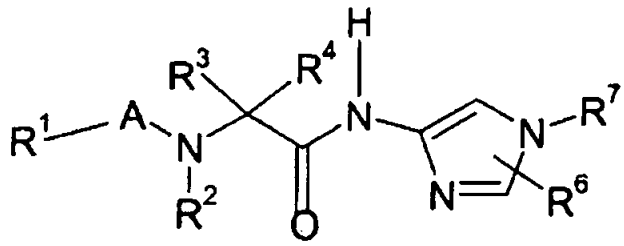
-OH, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -$S(O)_nR^{11}$ y -$S(O)_nNR^{11}R^{12}$;

en el que R^{11} y R^{12} en cada caso se seleccionan independientemente cada uno entre H, -alquilo C_1 - C_8, -cicloalquilo C_3 - C_8, -cicloalquenilo C_4 - C_8, bi- o tricicloalquilo (C_5 - C_{11}), bi- o tricicloalquenilo (C_7 - C_{11}), heterocicloalquilo de (entre 3 y 8 miembros), -arilo C_6 - C_{10} y -heteroarilo de (entre 5 y 14 miembros), en el que dicho alquilo de R^{11} está opcional e independientemente sustituido con entre uno y tres sustituyentes seleccionados independientemente entre - OH, - CN y cicloalquilo C_3 - C_8, y en el que cada átomo de hidrógeno de dicho alquilo está opcional e independientemente reemplazado con un átomo halo, y en el que dicho cicloalquilo, cicloalquenilo, heterocicloalquilo, arilo y heteroarilo de R^{11} están cada uno de ellos opcional e independientemente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre halo, alquilo C_1 - C_8 opcionalmente sustituido con entre uno a tres átomos halo, -OH, -CN y cicloalquilo C_3 - C_8; y

n es en cada caso un número entero seleccionado independientemente entre cero, 1 y 2;

o una sal farmacéuticamente aceptable del mismo.

12. Un compuesto de fórmula I



I

en la que A está ausente;

R^1 es -alquilo C_1 - C_{20}; en el que R^1 está sustituido independientemente con entre uno y seis sustituyentes seleccionados independientemente entre R^{1a};

en la que R^{1a} en cada caso se selecciona independientemente entre -alcoxi C_1 - C_6, -CN, -cicloalquilo C_3 - C_{15}, -cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

en la que dicho cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{1a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{1b};

en la que R^{1b} se selecciona en cada caso independientemente entre -OH, - alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -NR^9R^{10}, -C-(=O)NR^9R^{10}, -C(=O)R^{11}, -C(=O)OR^{12}, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o

tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

R^2 se selecciona entre H, -alquilo C_1 - C_6, -alquenilo C_2 - C_6, -cicloalquilo C_3 - C_8 y cicloalquenilo C_3 - C_8, en el que R^2 está opcional e independientemente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre alquilo C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, halo y -OH.

R^3 se selecciona entre H, -alquilo C_1 - C_6, -alquenilo C_2 - C_6, -alquinilo C_2 - C_6, -cicloalquilo C_3 - C_6, -cicloalquenilo C_5 - C_6 y heterocicloalquilo de (entre 3 y 8 miembros), -arilo C_6 - C_{14} y heteroarilo de (entre 5 y 14 miembros), en el que dicho alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquenilo, heterocicloalquilo, arilo o heteroarilo están cada uno de ellos opcional e independientemente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre alcoxi C_1 - C_4, halo, -OH, -S alquilo (C_1 - C_4), -alquilo (C_1 - C_4), $-C(=O)OR^9$, $-SO_2R^9$ y heterocicloalquilo de (entre 3 y 8 miembros) en el que dicho alquilo, alcoxi, y heterocicloalquilo puede estar adicionalmente sustituido con uno a seis halo;

R^4 es H, alquilo C_1 - C_6 o halo;

o R^3 y R^4 pueden junto con el átomo de carbono al que están unidos opcionalmente formar un resto seleccionado entre ciclopropilo, ciclobutilo, ciclopentilo, ciclohexilo, morfolino, piperidino, pirrolidino, tetrahidrofuranilo y perhidro-2H-pirano, en el que dicho resto formado por R^3 y R^4 está opcionalmente sustituido con entre uno a tres sustituyentes seleccionados

independientemente entre -alquilo C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, halo, -OH, -CN y alilo;

R^6 se selecciona entre H, -alquilo C_1 - C_6, -alquileno C_2 - C_6, -alcoxi C_1 - C_6, halo, -CN, -cicloalquilo C_3 - C_{12}, -cicloalquenilo C_4 - C_{12}, heteroarilo de (entre 5 y 10 miembros) y -arilo C_6 - C_{10}, en el que dicho alquilo, alquileno y alcoxi de R^6 están cada uno de ellos opcional e independientemente sustituidos con entre uno a tres sustituyentes seleccionados independientemente entre halo y -CN, y en el que dicho cicloalquilo, cicloalquenilo, heteroarilo y arilo de R^6 están cada uno de ellos opcional e independientemente sustituidos con entre uno a tres sustituyentes seleccionados independientemente entre -alquilo C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_4 opcionalmente sustituido con entre uno a tres átomos halo, halo y -CN;

R^7 se selecciona entre H, -alquilo C_1 - C_{20}, -alcoxi C_1 - C_{20}, -hidroxialquilo C_1 - C_{20}, -cicloalquilo C_3 - C_{12}, -cicloalquenilo C_4 - C_{12}, bi- o tricicloalquilo (C_5 - C_{20}), bi- o tricicloalquenilo (C_7 - C_{20}), -heterocicloalquilo de (entre 3 y 12 miembros), -heterobi o o heterotricicloalquilo de (entre 7 y 20 miembros) , -arilo C_6 - C_{14}, y -heteroarilo de (entre 5 y 15 miembros) en el que dichos alquilo, alquenilo, alquinilo, alcoxi, alquenoxi, alquinoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^7están cada uno de ellos opcional e independientemente sustituido con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{7a};

en la que R^{7a} en cada caso se selecciona independientemente entre -OH, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -

alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alquilo, alquenilo, alquinilo, alcoxi, alquenoxi, alquinoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{7a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{7b};

en la que R^{7b} en cada caso se selecciona independientemente entre -OH, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -NR^9R^{10}, -$C(=O)NR^9R^{10}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -SO_2-NR^9R^{10}, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

o R^6 y R^7 pueden junto con los átomos de carbono y nitrógeno a los que están respectivamente unidos opcionalmente formar un anillo heterocicloalquilo de (entre 5 y 8 miembros), un anillo heterocicloalquenilo de (entre 5 y 8 miembros) o un anillo heteroarilo de (entre 6 y 8 miembros) , en el que dichos anillos heterocicloalquilo, heterocicloalquenilo y heteroarilo están opcional e independientemente sustituidos cada uno con entre uno a tres sustituyentes

seleccionados independientemente entre halo, -alquilo C_1 - C_6, opcionalmente sustituido con entre uno a tres átomos halo, -alcoxi C_1 - C_6 opcionalmente sustituido con entre uno a tres átomos halo, -hidroxialquilo C_1 - C_6, -OH, -$(CH_2)_{cero\text{ - }10}$ NR^9R^{10}, -$(CH_2)_{cero\text{ - }10}$ $C(=O)NR^9R^{10}$, -$SO_2NR^9R^{10}$ y cicloalquilo C_3 - C_{12};

R^9 y R^{10} en cada caso se seleccionan cada uno de ellos independientemente entre H, -OH, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6 -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alquilo, alquenilo, alquinilo, alcoxi, alquenoxi, alquinoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^9 y R^{10} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{10a};

en la que R^{10a} en cada caso se selecciona independientemente entre -OH, halo, -alcoxi C_1 - C_6, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{12}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, -cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), -bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros); en la que dicho alcoxi, cicloalquilo, cicloalquenilo, bi- o tricicloalquilo, bi- o

tricicloalquenilo, heterocicloalquilo, arilo, heteroarilo, ariloxi y heteroariloxi de R^{10a} están cada uno opcionalmente independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre el grupo R^{10b};

en la que R^{10b} en cada caso se selecciona independientemente entre -OH, halo, -alquilo C_1 - C_{12}, -alquenilo C_2 - C_{12}, -alquinilo C_2 - C_{12}, -alcoxi C_1 - C_6, -alcoxialquilo C_1 - C_{12}, -hidroxialquilo C_1 - C_{12}, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, halo, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, -$C(=O)R^{11}$, -$C(=O)OR^{11}$, -SO_2-$NR^{11}R^{12}$, -$S(O)_n$-R^{11}, -cicloalquilo C_3 - C_{15}, - cicloalquenilo C_4 - C_{15}, -bi- o tricicloalquilo (C_5 - C_{11}), - bi- o tricicloalquenilo (C_7 - C_{11}), -heterocicloalquilo (de 4 a 20 miembros), -arilo C_6 - C_{15}, -heteroarilo (de 5 a 15 miembros), ariloxi C_6 - C_{15}, y -heteroariloxi (de 5 - 15 miembros);

o NR^9R^{10} puede formar un heterocicloalquilo de (entre 4 y 20 miembros), heterobi- o tricicloalquilo de (entre 5 y 18 miembros), heterobi- o tricicloalquenilo de (entre 5 y 18 miembros), o heteroarilo de (entre 5 y 15 miembros), en el que dicho heterocicloalquilo, heterobi- o tricicloalquilo, heterobi- o tricicloalquenilo o heteroarilo están opcionalmente e independientemente sustituidos con entre uno y seis sustituyentes seleccionados independientemente entre -alquilo C_1 - C_6, -alquenilo C_2 - C_6, - alquenilo C_2 - C_6, - alcoxi C_1 - C_6, -alquenoxi C_2 - C_6, -alquinoxi C_2 - C_6, - hidroxialquilo C_1 - C_6, - hidroxialquenilo C_2 - C_6, - hidroxialquenilo C_2 - C_6, halo, -OH, -CN, -NO_2, -$NR^{11}R^{12}$, -$C(=O)NR^{11}R^{12}$, - $C(=O)R^{11}$, -$C(=O)OR^{11}$, - $S(O)_nR^{11}$ y -$S(O)_nNR^{11}R^{12}$;

R^{11} y R^{12} en cada caso se seleccionan independientemente cada uno entre H, alquilo C_1 - C_8, cicloalquilo C_3 - C_8, cicloalquenilo C_4 - C_8, bi- o tricicloalquilo (C_5 - C_{11}), bi- o tricicloalquenilo (C_7 - C_{11}), heterocicloalquilo de

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(entre 3 y 8 miembros), arilo C_6 - C_{10} y heteroarilo de (entre 5 y 14 miembros), en el que dicho alquilo de R^{11} está opcional e independientemente sustituido con entre uno y tres sustituyentes seleccionados independientemente entre -OH, - CN y cicloalquilo C_3 - C_8, y en el que cada átomo de hidrógeno de dicho alquilo está opcional e independientemente reemplazado con un átomo halo, y en el que dicho cicloalquilo, cicloalquenilo, heterocicloalquilo, arilo y heteroarilo de R^{11} están cada uno de ellos opcional e independientemente sustituido con entre uno a tres sustituyentes seleccionados independientemente entre halo, alquilo C_1 - C_8 opcionalmente sustituido con entre uno a tres átomos halo, -OH, -CN y cicloalquilo C_3 - C_8; y

n es en cada caso un número entero seleccionado independientemente entre cero, 1 y 2;

o una sal farmacéuticamente aceptable del mismo.

13. Un compuesto seleccionado entre el grupo constituido por:

{1-[2-(3-etoxi-propilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(octahidro-pirazinol[1,2-a]azepin-2-il)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico,

{1-[2-([1,4]-dioxan-2-ilmetil-metilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(2-metoxi-1-metil-etilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3-oxo-piperazin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(2-bencilamino-etil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3-butoxi-propilamino)etil)]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-((1R,2S)-2-hidroximetil-ciclohexilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-(4aS,8aS)-2-(octahidro-isoquinolin-2-il)etil]-1H-imidazol-4-il}amida del ácido 2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3-isopropoxi-propilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(octahidro-isoquinolin-2-il)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3,4,5,6-tetrahidro-2H-[4,4']bipiridinil-1-il)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(2-hidroxi-2-fenil-etilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(indan-1-ilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(bencil-metilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(indan-2-ilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3,4-dihidro-1H-isoquinolin-2-il)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(2-propoxi-etilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-

difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3-bencil-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3-piridin-2-il-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(metil-piridin-4-ilmetil-amino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

(1-{2-[(2-metanosulfonil-etil)metil-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2- [2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(2-terc-butoxi-etilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3-piridin-4-il-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(2-fluoro-bencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(3-fluoro-bencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(4-metilbencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(4-metoxibencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(4-terc-butil-bencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(1-pirrolidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(1-dimetilaminometil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

[1-(1-piperidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(1-morfolin-4-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

(1-{1-[((2R,6S)-2,6-dimetil-morfolin-4-il)metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

(1-{1-[(2,2,2-trifluoro-etilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

(1-{1-[((R)-1-ciclohexil-etilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

[1-(1-pirrolidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-[(2,2-dimetil-propilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

(1-{1-[(2,2,2-trifluoroetilamino)metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-[(2,2-dimetil-propilamino)metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-[((R)-1-ciclohexil-etilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

[1-(1-dimetilaminometil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

[1-(1-piperidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-(6,8-

difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

[1-(1-morfolin-4-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

(1-{1-[((2R, 6S)-2,6-dimetil-morfolin-4-il)metil]ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

{1-[2-((R)-1-ciclohexil-etilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

(1-{1,1-dimetil-2-[(tetrahidropiran-4-ilmetil)amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

(1-{2-[(1-hidroxi-ciclohexilmetil)-amino]-1,1-dimetil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

(1-{2-[(4-hidroxi-tetrahidro-piran-4-ilmetil)-amino]-1,1-dimetil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

{1-[2-(2-metoxi-2-metilpropilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)- pentanoico;

(1-{1,1-dimetil-2-[(3-metiloxetan-3-ilmetil)-amino]etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)- pentanoico;

{1-[2-(ciclohexilmetil-amino)-1,1-dimetil-etil]-1H-imidazol- 4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)- pentanoico;

{1-[2-((R)-1-ciclohexiletil-amino)-1,1-dimetil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]- pentanoico;

(1-{1,1-dimetil-2-[(tetrahidro-piran-4-ilmetil)-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[3-((S)-1-fenil-etilamino)-butil]-1H-imidazol- 4-il}amida del ácido (S)-2-(6,8-

difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1-H-imidazol-4-il]amida del ácido (S)-2-(diciclopropilmetil-amino)-pentanoico;

[1-(1-hidroximetil-ciclobutil)-1-H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(2-hidroximetil-ciclobutil)-1-H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(1-hidroximetil-ciclobutil)-1-H-imidazol-4-il]amida del ácido (S)-2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(2,4- difluoro-fenil)-2-hidroxietilamino]-pentanoico;

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,4- difluoro-fenil)-2-hidroxietilamino]-pentanoico;

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)-2-hidroxietilamino]-pentanoico;

{1-[2-((2R,6S)-2,6-dimetil-morfolin-4-il)-1,1-dimetil-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-[2- (2,4-difluoro-fenil)-2-hidroxietilamino]-pentanoico;

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido (S)-2-[(1-hidroxiciclohexilmetil)amino]-pentanoico;

{1-[3-((R)-1-fenil-etilamino)propil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(3-metil-bencilamino)-propil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(2-hidroxi-2-fenil-etilamino)-propil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(2-cloro-bencilamino)-propil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(3,4-dihidro-1H-isoquinolin-2-il)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(indan-2-ilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(1-metoximetil-propilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(4-cloro-bencilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(2-metilbencilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(2-metoxietilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{3-[(piridin-3-ilmetil)amino]-propil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-((S)-1-p-tolil-etilamino)propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(4-metoxibencilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(ciclopropilmetilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(4-metilbencilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1-metil-1-(metilfenetil-carbamoil)-etil]-1H-imidazol-4-il}amida del ácido (S)-

2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1-(1,3-dihidro-isobenzofuran-5-ilcarbamoil)-1-metil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1-(indan-1-ilcarbamoil)-1-metil-etil]-1H-imidazol-4- il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1,1-dimetil-2-oxo-2-(3-piridin-4-il-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

(1-{1-[2-(3-fluoro-fenil)-etilcarbamoil]-1-metiletil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[2-(3-ciano-piperidin-1-il)-1,1-dimetil-2-oxo-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-metil-1-[metil-(tetrahidro-piran-2-ilmetil)carbamoil]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-[etil-(2-pirazol-1-il-etil)carbamoil]-1-metiletil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1,1-dimetil-2-oxo-2-(2-fenil-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-[(furan-2-ilmetil)carbamoil]-1-metiletil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{2-[3-(acetil-metil-amino)pirrolidin-1-il]-1,1-dimetil-2-oxo-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1-metil-1-((3R,4S)-4-metilsulfanil-tetrahidro-furan-3-ilcarbamoil)etil]-1H-

imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[2-(4-acetil-[1,4]diazepan-1-il)-1,1-dimetil-2-oxo-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-metil-1-[1-(1-metil-1H-pirazol-4-il)etilcarbamoil]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1-(3-metoxi-propilcarbamoil)-1-metiletil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-metil-1-[(3-metil-[1,2,4]oxadiazol-5-ilmetil)carbamoil]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-[(2-ciano-etil)-metilcarbamoil]-1-metil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1,1-dimetil-2-(3-metil-5,6-dihidro-8H-[1,2,4]triazolo[4,3-a]pirazin-7-il)-2-oxo-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

(1-{1-metil-1-[metil-(1-metil-1H-imidazol-2-ilmetil)carbamoil]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-[(2-dietilamino-etil)metil-carbamoil]-1-metil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)propionilamino]-imidazol-1-il}-N-indan-1-il-isobutiramida;

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1- [1,1-dimetil-2-oxo-

2-(3-piridin-4-il-pirrolidin-1-il)etil]-1H-imidazol-4-il}- propionamida;

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1- [2- (4-hidroximetil-4-metilpiperidin-1-il)-1,1-dimetil-2-oxo-etil]-1H-imidazol-4-il} propionamida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)propionilamino]-imidazol-1-il}-N-metil-N-fenetil-isobutiramida;

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)propionilamino]-imidazol-1-il}-N-etil-N-(2-pirazol-1-il-etil)-isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1-[2-(4-hidroximetil-4-metil-piperidin-1-il)-1,1-dimetil-2-oxo-etil]-1H-imidazol-4-il}-propionamida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-(4-metilbencil)-isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-(1,3-dihidro-isobenzofuran-5-il)-isobutiramida;

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1-[1,1-dimetil-2-oxo-2-(2-fenilpirrolidin-1-il)-etil]-1H-imidazol-4-il}-propionamida;

(S)-N-{1-[2-(3-ciano-piperidin-1-il)-1,1-dimetil-2-oxo-etil]-1H-imidazol-4-il}-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionamida;

(S)-N-(1-{2-[3-(acetil-metil-amino)-pirrolidin-1-il]-1,1-dimetil-2-oxo-etil}-1H-imidazol-4-il)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionamida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-((1R, 2S)-2-hidroximetil-ciclohexil)isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-(3-metil-[1,2,4]oxadiazol-5-ilmetil)isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-

imidazol-1-il}-N-((S)-2-metoxi-1-metil-etil)isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-(3-metoxipropil)isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-[1-(1-metil-1H-pirazol-4-il)-etil]-isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-(3-imidazol-1-il-propil)-isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-(3-morfolin-4-il-propil)-isobutiramida;

[1-(3-metil-oxetan-3-ilmetil)-1H-imidazol-4-il]-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

[1-(3-metil-oxetan-3-ilmetil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[1-(4-trifluorometilfenil)etil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1-(4-trifluorometil-fenil)-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(2-pirrolidin-1-ilmetilciclobutil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(2-pirrolidin-1-ilmetilciclobutil)-1H-imidazol-4-il]-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1,1-dimetil-2-[(tetrahidro-piran-4-ilmetil)-amino]etil}-1H-imidazol-4-il)-amida del ácido (S)-2- (1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[2-(2-etoxi-etilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1-[2-(2-etoxi-etilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-propionamida;

(1-{2-[(1-hidroxi-ciclohexilmetil)-carbamoil]-1,1-dimetil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-[(1-hidroxi-ciclohexilmetil)-carbamoil]-1-metil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

(1-{1-metil-1-[(tetrahidro-piran-4-ilmetil)-carbamoil]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

{1-[1-metil-1-(2-metil-bencilcarbamoil)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1-(2-metoxi-1-metil-etilcarbamoil)-1-metil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

(1-{1-metil-2-[(tetrahidropiran-4-ilmetil)amino]-etil}-1H-imidazol-4- il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

(1-{2-[(1-hidroxi-ciclohexilmetil)-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{2-[(4-hidroxi-tetrahidropiran-4-ilmetil)-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

(1-{2-[(tetrahidro-piran-4-ilmetil)-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{2-[(3-metil-oxetan-3-ilmetil)-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{2-[(1-hidroxi-ciclohexilmetil)-amino]-1-metil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

{1-[2-(2-etoxi-etilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

[1-(3-bencilamino-propil)-1H-imidazol-4-il]amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

(1-{1,1-dimetil-3-[(piridin-2-ilmetil)amino]-propil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1,1-dimetil-3-((S)-2,2,2-trifluoro-1-fenil-etilamino)propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1,1-dimetil-3-((R)-1-fenil-etilamino)propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[2-((2R,6S)-2,6-dimetilmorfolin-4-il)-1,1-dimetiletil]-1H-imidazol-4- il}amida del ácido (S)-2-(2-trifluorometil-bencilamino)-pentanoico;

{1-[2-((2R,6S)-2,6-dimetilmorfolin-4-il)-1,1-dimetiletil]-1H-imidazol-4- il}amida del ácido (S)-2-{[(2-fluoro-3-trifluorometil-fenil)metil]-amino}pentanoico;

(S)-2-[2-(3,5-difluoro-fenil)acetilamino]-N-[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-2-fenilacetamida;

(S)-2-[2-(3,5-difluoro-fenil)acetilamino]-N-{1-[2-((2S,6R)-2,6-dimetil-morfolin-4-il)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-fenilacetamida;

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1-[2-(2,2-dimetil-propilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-fenilacetamida;

(1-indan-1-il-1H-imidazol-4-il)-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico;

[(S)-1-((1S,2R)-2-hidroxi-indan-1-il)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico;

[(R)-1-((1R,2S)-2-hidroxi-indan-1-il)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico;

{1-[1-(4-fluorofenil)-2-hidroxi-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico;

{(R)-1-[(R)-1-(4-fluoro-fenil)-2-hidroxi-etil]-1H-imidazol-4-il}-amida del ácido (S)-2- [2-(3,5-difluoro-fenil)acetilamino]pentanoico;

[1-(2-hidroximetil-fenil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico;

(S)-2-[2-(3,5-difluoro-fenil)acetilamino]-N-{1-[2-(2,2-dimetil-propilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-fenil-acetamida;

{(S)-1-[2-(2,2-dimetilpropilamino)-1-fenil-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{(S)-1-[2-(2,2-dimetilpropilamino)-1-fenil-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

2-[2-(3,5-difluoro-fenil)acetilamino]-N-{1-[2-(2,2-dimetilpropilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-(4-fluoro-fenil)acetamida;

2-[2-(3,5-difluoro-fenil)acetilamino]-N-{1-[2-(2,2-dimetilpropilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-piridin-3-il-acetamida;

(1-{2-[(2,2-dimetil-propilamino)-metil]-fenil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{2-[(2-hidroxi-butilamino)-metil]-fenil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[2-(3-etoxi-propilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(2-fluoro-bencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-

fenil)acetilamino]-pentanoico;

[1-(3-fluoro-bencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(4-metilbencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(4-metoxibencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(4-terc-butil-bencil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(1-hidroximetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(2-hidroximetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(1-pirrolidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2- [2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-((R)-1-ciclohexil-etilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[2-((R)-1-ciclohexil-etilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(2,4-difluoro-fenil)-2-hidroxietilamino]-pentanoico;

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,4-difluoro-fenil)-2-hidroxietilamino]-pentanoico;

(1-{1,1-dimetil-2-[(tetrahidro-piran-4-ilmetil)-amino]-etil}-1H-imidazol-4-il)-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-

pentanoico;

(1-{1,1-dimetil-2-[(tetrahidro-piran-4-ilmetil)-amino]-etil}-1H-imidazol-4-il)-amida del ácido ((S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[3-((S)-1-fenil-etilamino)-butil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

[1-(3-metil-oxetan-3-ilmetil)-1H-imidazol-4-il]-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

[1-(3-metil-oxetan-3-ilmetil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1-H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)-2-hidroxietilamino]-pentanoico;

{1-[2-((2R,6S)-2,6-dimetilmorfolin-4-il)-1,1-dimetiletil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(2,4-difluorofenil)-2-hidroxi-etilamino]-pentanoico;

{1-[2-(octahidro-pirazino[1,2-a]azepin-2-il)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-([1,4]-dioxan-2-ilmetil-metilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(2-metoxi-1-metil-etilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3-oxo-piperazin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(2-bencilamino-etil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3-butoxi-propilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-((1R,2S)-2-hidroximetil-ciclohexilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[(4aS, 8aS)-2-(octahidro-isoquinolin-2-il)etil]-1H-imidazol-4-il}amida del ácido 2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3-isopropoxi-propilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(octahidro-isoquinolin-2-il)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3,4,5,6-tetrahidro-2H-[4,4']bipiridinil-1-il)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(2-hidroxi-2-fenil-etilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(indan-1-ilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(bencil-metilamino)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(indan-2-ilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3,4-dihidro-1H-isoquinolin-2-il)etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(2-propoxi-etilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3-bencil-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3-piridin-2-il-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-

(3,5- difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(metil-piridin-4-ilmetil-amino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

(1-{2-[(2-metanosulfonil-etil)metil-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2- [2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(2-terc-butoxi-etilamino)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(3-piridin-4-il-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-amida del ácido (S)-2-[(1-hidroxiciclohexilmetil)amino]-pentanoico;

(S)-2-[2-(3,5-difluoro-fenil)acetilamino]-N-[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1H-imidazol-4-il]-2-fenilacetamida;

[1-(1,1-dimetil-2-pirrolidin-1-il-etil)-1-H-imidazol-4-il]amida del ácido (S)-2-(diciclopropilmetil-amino)-pentanoico;

{1-[3-((R)-1-fenil-etilamino)propil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{2-[(1-hidroxi-ciclohexilmetil)-amino]-1,1-dimetil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

(S)-2-[2-(3,5-difluoro-fenil)acetilamino]-N-{1-[2-((2S,6R)-2,6-dimetil-morfolin-4-il)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-fenilacetamida;

(1-{2-[(4-hidroxi-tetrahidro-piran-4-ilmetil)-amino]-1,1-dimetil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

[1-(1-dimetilaminometil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-

difluoro-fenil)acetilamino]-pentanoico;

[1-(1-piperidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

[1-(1-morfolin-4-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

(1-{1-[((2R,6S)-2,6-dimetil-morfolin-4-il)metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

(1-{1-[(2,2,2-trifluoro-etilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

(1-{1-[((R)-1-ciclohexil-etilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]-pentanoico;

[1-(1-hidroximetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

[1-(1-pirrolidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il)amida del ácido (S)-2-[2-(5,7-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-[(2,2-dimetil-propilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1-[2-(2,2-dimetil-propilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-fenil-acetamida;

{1-[1-(4-trifluorometilfenil)etil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1-(4-trifluorometil-fenil)-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]-pentanoico;

{1-[2-(2-metoxi-2-metil-propilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}- amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)- pentanoico;

(1-{1,1-dimetil-2-[(3-metiloxetan-3-ilmetil)-amino]etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)- pentanoico;

{1-[2-(ciclohexilmetil-amino)-1,1-dimetil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)- pentanoico;

(1-{1-metil-2-[(tetrahidropiran-4-ilmetil)amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-indan-1-il-1H-imidazol-4-il)-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico;

[(S)-1-((1S, 2R)-2-hidroxi-indan-1-il)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico;

[(R)-1-((1R,2S)-2-hidroxi-indan-1-il)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico;

[1-(2-pirrolidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico;

[1-(2-pirrolidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)pentanoico;

{1-[1-(4-fluorofenil)-2-hidroxi-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-[2-(3,5-difluoro-fenil)acetilamino]pentanoico;

{1-[3-(3-metil-bencilamino)-propil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(2-hidroxi-2-fenil-etilamino)-propil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(2-cloro-bencilamino)-propil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(3,4-dihidro-1H-isoquinolin-2-il)-propil]-1H-imidazol-4-il}amida del ácido

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(indan-2-ilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(1-metoximetil-propilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(4-cloro-bencilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(2-metilbencilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(2-metoxietilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{3-[(piridin-3-ilmetil)amino]-propil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-((S)-1-p-tolil-etilamino)propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(4-metoxibencilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(ciclopropilmetilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[3-(4-metilbencilamino)-propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{2-[(1-hidroxi-ciclohexilmetil)-carbamoil]-1,1-dimetil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1,1-dimetil-2-[(tetrahidropiran-4-ilmetil)amino]-etil}-1H-imidazol-4-il)amida

del ácido (S)-2-(1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

(1-{2-[(1-hidroxi-ciclohexilmetil)-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

(1-{1-[(2,2,2-trifluoro-etilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

(1-{1-[(2,2-dimetilpropilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

(1-{1-[((R)-1-ciclohexil-etilamino)-metil]-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

[1-(1-dimetilaminometil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

[1-(1-piperidin-1-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

[1-(1-morfolin-4-ilmetil-ciclobutil)-1H-imidazol-4-il]amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-[((2R,6S)-2,6-dimetil-morfolin-4-il)metil-ciclobutil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

(1-{2-[(4-hidroxi-tetrahidro-piran-4-ilmetil)-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidro-naftalen-2-ilamino)-pentanoico;

(1-{2-[(tetrahidro-piran-4-ilmetil)-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{2-[(3-metil-oxetan-3-ilmetil)-amino]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{2-[(1-hidroxi-ciclohexilmetil)-amino]-1-metil-etil}-1H-imidazol-4- il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

(1-{1,1-dimetil-3-[(piridin-2-ilmetil)amino]-propil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-[(1-hidroxi-ciclohexilmetil)-carbamoil]-1-metil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

{1-[2-((2R,6S)-2,6-dimetilmorfolin-4-il)-1,1-dimetiletil]-1H-imidazol-4- il}amida del ácido (S)-2-{[(2-fluoro-3-trifluorometil-fenil)metil]amino}-pentanoico;

{1-[1,1-dimetil-3-((S)-2,2,2-trifluoro-1-fenil-etilamino)propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1,1-dimetil-3-((R)-1-fenil-etilamino)propil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[2-((2R,6S)-2,6-dimetilmorfolin-4-il)-1,1-dimetiletil]-1H-imidazol-4- il}amida del ácido (S)-2-(2-trifluorometil-bencilamino)-pentanoico;

(1-{1-metil-1-[(tetrahidro-piran-4-ilmetil)carbamoil]-etil}-1H-imidazol-4- il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

{1-[2-(2-etoxi-etilamino)-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{(R)-1-[(R)-1-(4-fluoro-fenil)-2-hidroxi-etil]-1H-imidazol-4-il}-amida del ácido (S)-2- [2-(3,5-difluoro-fenil)acetilamino]pentanoico;

[1-(2-hidroximetil-fenil)-1H-imidazol-4-il]-amida del ácido (S)-2-[2-(3,5- difluoro-fenil)acetilamino]pentanoico;

{1-[2-(2-etoxi-etilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1-[2-(2-etoxi-etilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-propionamida;

(S)-2-[2-(3,5-difluoro-fenil)acetilamino]-N-{1-[2-(2,2-dimetil-propilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-fenil-acetamida;

{1-[1-metil-1-(2-metil-bencilcarbamoil)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1-(2-metoxi-1-metil-etilcarbamoil)-1-metil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{(S)-1-[2-(2,2-dimetil-propilamino)-1-fenil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

[1-(3-bencilamino-propil)-1H-imidazol-4-il]amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{2-[(2,2-dimetil-propilamino)-metil]-fenil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{(S)-1-[2-(2,2-dimetil-propilamino)-1-fenil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{2-[(2-hidroxi-butilamino)-metil]-fenil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

2-[2-(3,5-difluoro-fenil)acetilamino]-N-{1-[2-(2,2-dimetil-propilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-piridin-3-il-acetamida;

2-[2-(3,5-difluoro-fenil)acetilamino]-N-{1-[2-(2,2-dimetil-propilamino)-1,1-dimetil-etil]-1H-imidazol-4-il}-2-(4-fluoro-fenil)-acetamida;

{1-[1-metil-1-(metilfenetil-carbamoil)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1-(1,3-dihidro-isobenzofuran-5-ilcarbamoil)-1-metil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1-(indan-1-ilcarbamoil)-1-metil-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1,1-dimetil-2-oxo-2-(3-piridin-4-il-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

(1-{1-[2-(3-fluoro-fenil)-etilcarbamoil]-1-metiletil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)propionilamino]-imidazol-1-il}-N-indan-1-il-isobutiramida;

{1-[2-(3-ciano-piperidin-1-il)-1,1-dimetil-2-oxo-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-metil-1-[metil-(tetrahidro-piran-2-ilmetil)carbamoil]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-[etil-(2-pirazol-1-il-etil)carbamoil]-1-metiletil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1,1-dimetil-2-oxo-2-(2-fenil-pirrolidin-1-il)-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)p-N-{1-[1,1-dimetil-2-oxo-2-(3-piridin-4-il-pirrolidin-1-il)etil]-1H-imidazol-4-il}- propionamida;

(1-{1-[(furan-2-ilmetil)carbamoil]-1-metiletil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{2-[3-(acetil-metil-amino)pirrolidin-1-il]-1,1-dimetil-2-oxo-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[1-metil-1-((3R,4S)-4-metilsulfanil-tetrahidro-furan-3-ilcarbamoil)etil]-1H-

imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

{1-[2-(4-acetil-[1,4]diazepan-1-il)-1,1-dimetil-2-oxo-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)propionilamino]-imidazol-1-il}-N-[2-(3-fluorofenil)-etil]-isobutiramida;

(1-{1-metil-1-[1-(1-metil-1H-pirazol-4-il)etilcarbamoil]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8 Difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)propionilamino]-imidazol-1-il}-N-metil-N-fenetil-isobutiramida;

{1-[1-(3-metoxi-propilcarbamoil)-1-metiletil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-metil-1-[(3-metil-[1,2,4]oxadiazol-5-ilmetil)carbamoil]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(1-{1-[(2-ciano-etil)-metilcarbamoil]-1-metil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)propionilamino]-imidazol-1-il}-N-etil-N-(2-pirazol-1-il-etil)-isobutiramida;

{1-[1,1-dimetil-2-(3-metil-5,6-dihidro-8H-[1,2,4]triazolo[4,3-a]pirazin-7-il)-2-oxo-etil]-1H-imidazol-4-il}amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

(1-{1-metil-1-[metil-(1-metil-1H-imidazol-2-ilmetil)carbamoil]-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-pentanoico;

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1-[2- (4-hidroximetil-4-metilpiperidin-1-il)-1,1-dimetil-2-oxo-etil]-1H-imidazol-4-il} propionamida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)propionilamino]-imidazol-1-il}-N-(4-metil-bencil)-isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-(1,3-dihidro-isobenzofuran-5-il)-isobutiramida

(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-N-{1-[1,1-dimetil-2-oxo-2-(2-fenilpirrolidin-1-il)-etil]-1H-imidazol-4-il}-propionamida;

(1-{1-[(2-dietilamino-etil)metil-carbamoil]-1-metil-etil}-1H-imidazol-4-il)amida del ácido (S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- pentanoico;

(S)-N-{1-[2-(3-ciano-piperidin-1-il)-1,1-dimetil-2-oxo-etil]-1H-imidazol-4-il}-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionamida;

(S)-N-(1-{2-[3-(acetil-metil-amino)-pirrolidin-1-il]-1,1-dimetil-2-oxo-etil}-1H-imidazol-4-il)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)- propionamida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-((1R, 2S)-2-hidroximetil-ciclohexil)isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-(3-metil-[1,2,4]oxadiazol-5-ilmetil)isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-((S)-2-metoxi-1-metil-etil)isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-(3-metoxipropil)isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-[1-(1-metil-1H-pirazol-4-il)-etil]-isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-

imidazol-1-il}-N-(3-imidazol-1-il-propil)-isobutiramida;

2-{4-[(S)-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-ilamino)-propionilamino]-imidazol-1-il}-N-(3-morfolin-4-il-propil)-isobutiramida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(1-hidroxiciclohexil)metil]amino}-1,1-dimetiletil)-1H-imidazol-4-il]-L-norvalinamida

N-2-[(3,5-difluorofenil)acetil]-N-{1-[1-(piperidin-1-ilmetil)ciclobutil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[1-(pirrolidin-1-ilmetil)ciclobutil]-1H-imidazol- 4-il}-L-norvalinamida;

N-2-[(3,5-difluorofenil)acetil]-N-[1-(1-{[(2,2-dimetilpropil)amino]metil}ciclobutil)-1H-imidazol-4-il]-L-norvalinamida;

N-2-[(3,5-difluorofenil)acetil]-N-[1-(1-{[(2,2-dimetilpropil)amino]metil}ciclobutil)-1H-imidazol-4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(1-{[(2,2-dimetilpropil) amino]metil}ciclobutil)-1H-imidazol-4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{1,1-dimetil-2-[(2-metilbencil)amino]-2- oxoetil}-1H-imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{1-metil-2-[(tetrahidro-2H-piran-4- ilmetil)amino]etil}- 1H-imidazol-4-il)- L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(3-metoxipropil)amino]-1,1-dimetil-2- oxoetil}-1H-imidazol-4-il)-L- norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2-

hidroxibutil)amino]-metil}fenil)-1H- imidazol-4-il]-L-norvalinamida;

3-{[4-({N-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalil}amino)-1H-imidazol-1-il]metil}azetidina-1-carboxilato de terc-butilo

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{[1-(2,2-dimetilpropil)azetidin-3-il]-metil}-1H- imidazol-4-il)-L-norvalinamida;

2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-N-(2,2-dimetilpropil)-2-metilpropanamida;

N-(2-clorobencil)-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2- fenilacetil}amino)-1H-imidazol-1-il]- 2-metilpropanamida;

2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-N-(2,3-dihidro-1H-inden-1-il)-2-metilpropanamida;

N-[(1R)-1-ciclohexiletil]-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2- fenilacetil}amino)-1H-imidazol-1-il]- 2-metilpropanamida;

(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-N-{1-[1,1-dimetil-2-(3-metilpiperidin-1-il)- 2-oxoetil]-1H-imidazol-4-il}-2- fenilacetamida;

2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-2-metil-N-(2-metilciclohexil)propanamida;

(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-N-{1-[1,1-dimetil-2-(2-metilpiperidin-1-il)-2-oxoetil]-1H-imidazol-4-il}-2- fenilacetamida;

(2S)-N-(1-{2-[(1R,4S)-2-azabiciclo[2.2.1]hept-2-il]-1,1-dimetil-2-oxoetil}-1H-imidazol-4-il)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-

fenilacetamida;

2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-2-metil-N-(tetrahidro-2H-piran-4-il)propanamida;

(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-N-{1-[1,1-dimetil-2-oxo-2-(3-fenilpirrolidin-1-il)etil]-1H-imidazol- 4-il}-2-fenilacetamida;

N-(3,4-difluorobencil)-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2- fenilacetil}amino)-1H-imidazol-1-il]- 2-metilpropanamida;

(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-N-[1-(1,1-dimetil-2-oxo-2-pirrolidin-1- iletil)-1H-imidazol-4-il]-2-fenilacetamida;

2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]- N-(2,2-dimetilpropil)-2-metilpropanamida;

N-ciclohexil-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H- imidazol-1-il]-2-metilpropanamida;

2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-2-metil-N-(2-metilbencil)propanamida;

(2S)-N-(1-{2-[(1S,5R)-6-azabiciclo[3.2.1]oct-6-il]-1,1-dimetil-2-oxoetil}-1H-imidazol-4-il)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetamida;

N-(2,4-difluorobencil)-2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-2-metilpropanamida;

(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-N-{1-[1,1-dimetil-2-oxo-

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2-(3-piridin-4-ilpirrolidin-1-il)etil]-1H-imidazol-4-il}-2-fenilacetamida;

2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]- 2-metil-N-(4-metilciclohexil)propanamida;

2-[4-({(2S)-2-[(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)amino]-2-fenilacetil}amino)-1H-imidazol-1-il]-2-metil-N-(3,3,5,5-tetrametilciclohexil)propanamida;

N-2-(6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il)-N-(1-{1,1-dimetil-2-[(2-metilbencil)amino]-2- oxoetil}-1H-imidazol-4-il)-O-metil-L-serinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{[1-(2,2-dimetilpropil)pirrolidin-2-il]metil}-1H-imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{[1-(2,2-dimetilpropanoil)pirrolidin-2-il]metil}-1H-imidazol-4-il)-L-norvalinamida;

(2S)-2-{[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]amino}-N-{1-[1-(2,2-dimetilpropil)-2-oxopiperidin-3-il]-1H-imidazol-4- il}pentanamida;

(2S)-N-[1-(1-bencil-2-oxopiperidin-3-il)-1H-imidazol-4-il]-2-{[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]amino}pentanamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{[(2S)-1-(2,2-dimetilpropil)azetidin-2- il]metil}-1H-imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-({(2S)-1-[(2S)-2-hidroxibutil]azetidin-2-il}metil)-1H-imidazol-4-il)-L-norvalinamida;

3-{[4-({N-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalil}amino)-1H-imidazol-1- il]metil}-3-hidroxiazetidina-1-carboxilato de terc-butilo

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{[1-(2,2-dimetilpropil)-3-hidroxiazetidin-3-il]- metil}-1H-imidazol-4-il)-L-norvalinamida;

N-{1-[(3S,4R)-1-bencil-4-{2-[(2,2-dimetilpropil)amino]etil}pirrolidin-3-il]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2,2-dimetilpropil)amino]metil}-4,5-difluorofenil)-1H-imidazol-4-il]-L-norvalinamida;

N-{1-[2-({3-[acetil(metil)amino]pirrolidin-1-il}-metil)fenil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4- tetrahidronaftalen-2-il]-L-norvalinamida;

N-{1-[2-({[(1R,2R)-2- (benciloxi)ciclopentil]amino}metil)fenil]-1H-imidazol-4-il}-N-2-[(2S)-6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-(1-{2-[(4-acetil-1,4-diazepan-1-il)metil]fenil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(3-hidroxipiperidin-1-il)etil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1-etilpiperidin-3-il)metil]amino}metil)fenil]-1H-imidazol- 4-il}-L-norvalinamida;

N-{1-[2-({[(3R)-1-acetilpirrolidin-3-il]amino}metil)fenil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(4-etilpiperazin-1-il)metil]fenil}-1H- imidazol- 4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1S,2R)-2-hidroxi-

2,3-dihidro-1H- inden-1-il]amino}metil)fenil]-1H-imidazol- 4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-(morfolin-4-ilmetil)fenil]-1H- imidazol- 4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2-morfolin-4-iletil)amino]metil}fenil)-1H-imidazol- 4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-2-oxo-1,3-oxazinan-3-il)etil]amino}metil)fenil]-1H-imidazol- 4-il}-L-norvalinamida;

N-(1-{2-[(biciclo[1.1.1]pent-1-ilamino)metil]fenil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2-propoxietil)amino]metil}fenil)-1H-imidazol- 4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1-isobutirilpiperidin-3- il)metil]amino}metil)fenil]-1H-imidazol- 4-il}-L-norvalinamida;

N-{1-[2-({[(1R,2R)-2-(benciloxi)ciclohexil]amino}metil)fenil]-1H-imidazol-4-il}-N-2-[(2S)-6,8- difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(dimetilamino)-2-oxoetil]amino}metil)fenil]-1H-imidazol- 4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-(2,3-dihidro-1H-indol-1-ilmetil)fenil]-1H-imidazol-4-il}-L-norvalinamida;

N-[1-(2-{[(2,4-difluorobencil)amino]metil}fenil)-1H-imidazol-4-il]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(2-

fluorofenoxi)etil]amino}metil)fenil]-1H- imidazol-4-il}-L-norvalinamida;

N-{1-[2-({[2-(dietilamino)etil]amino}metil)fenil]-1H-imidazol-4-il]-N-2-[(2S)-6,8-difluoro- 1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(2-oxo-1,3-oxazolidin-3- il)etil]amino}metil)fenil]-1H-imidazol-4- il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(2-oxoimidazolidin-1- il)etil]amino}metil)fenil]-1H-imidazol-4- il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(3-metil-1H-pirazol-1-il)etil]amino}metil)fenil]-1H-imidazol-4- il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[1-(hidroximetil)pentil]amino}metil)fenil]-1H-imidazol-4- il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2-isopropoxietil)amino]metil}fenil)-1H- imidazol-4- il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1R)-1-(hidroximetil)propil]amino} metil)fenil]-1H-imidazol-4-il}-L-norvalinamida;

N-{1-[2-({[1-(4-clorobencil)-2-hidroxietil]amino}metil)fenil]-1H-imidazol-4-il}- N-2-[(2S)-6,8-difluoro- 1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1,3-dimetilpirrolidin-3- il)metil]amino}metil)fenil]-1H-imidazol- 4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1,3-dimetilpirrolidin-3- il)metil]amino}metil)fenil]-1H-imidazol- 4-il}-L-norvalinamida;

N-(1-{2-[(4-acetilpiperazin-1-il)metil]fenil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-

1,2,3,4- tetrahidronaftalen-2-il]-L-norvalinamida;

N-{1-[2-({[(1-terc-butil-5-oxopirrolidin-3-il)metil]amino}metil)fenil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2-metoxietil)amino]metil}fenil)-1H- imidazol- 4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2-etoxietil)amino]metil}fenil)-1H- imidazol- 4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(diisopropilamino)etil]amino}metil) fenil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[3-(1H-imidazol-1-il)propil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1S)-1-Hidroximetil)-2,2-dimetilpropil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1S)-1-metil-2-(metilamino)-2-oxoetil]amino}metil)fenil]-1H- imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(dimetilamino)-1-metiletil]amino}metilfenil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(3-metil-5,6-dihidro[1,2,4]triazolo[4,3-a]pirazin-7(8H)-il)metil]fenil}-1H-imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(3-metil-1,2,4-oxadiazol-5- il)metil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2-fenoxietil)amino]metil}fenil)-1H-imidazol-4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[metil(1-metilpirrolidin-3-il)amino]metil}fenil)-1H-imidazol-4-il]- L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2,2,2-trifluoroetil)amino]metil}fenil)- 1H-imidazol-4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1S,2S)-1-(hidroximetil)-2-metilbutil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(2-oxopirrolidin-1-il)etil]amino}metil)fenil]- 1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(2,3-dihidro-1H-inden-2-ilamino)metil]fenil} -1H-imidazol-4-il)-L-norvalinamida;

N-{1-[2-({[2-(acetilamino)etil]amino}metil)fenil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[2-(dimetilamino)etil]amino}metil)fenil]- 1H-imidazol-4-il}-L-norvalinamida;

N-{1-[2-({[(1R)-1-bencil-2-hidroxietil]amino}metil)fenil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2-metilciclohexil)amino]metil}fenil)-1H- imidazol-4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1S)-1-(hidroximetil)-2-metilpropil]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-(pirrolidin-1-ilmetil)fenil]-1H-imidazol- 4-il}-L-norvalinamida;

N-{1-[2-({[3-(benciloxi)-2-hidroxipropil]amino}metil)fenil]-1-H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2-hidroxi-3-fenoxipropil) amino]metil}fenil)-1H-imidazol-4-il]-L-norvalinamida;

N-(1-{2-[(terc-butilamino)metil]fenil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2- il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(5-metilisoxazol-3-il)metil] amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[({[(2R)-1-etilpirrolidin-2-il]metil}amino)metil]fenil}-1H-imidazol-4-il)-L-norvalinamida;

N-(1-{2-[({2-[butil(metil)amino]etil}amino)metil]fenil}-1H-imidazol-4-il)-N-2-[(2S)-6,8- difluoro-1,2,3,4-tetrahidronaftalen-2- il]-L-norvalinamida;

N-(1-{2-[({2-[butil(metil)amino]metil}amino)etil]fenil}-1H-imidazol-4-il)-N-2-[(2S)-6,8- difluoro-1,2,3,4-tetrahidronaftalen-2- il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(prop-2-in-1-ilamino)metil]fenil}-1H-imidazol- 4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(3-etilisoxazol-5-il)metil]amino}metil)fenil] -1H-imidazol-4-il}-L-norvalinamida;

N-{1-[2-({[2-(dietilamino)etil](metil)amino}metil)fenil]-1H-imidazol-4-il}-N-2-[(2S)-6,8- difluoro-1,2,3,4-tetrahidronaftalen-2- il]-L-norvalinamida;

N-[1-(2-{[(2-terc-butoxietil)amino]metil}fenil)-1H-imidazol-4-il]-N-2-[(2S)-6,8-difluoro- 1,2,3,4-tetrahidronaftalen-2-il]-L- norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[({[(2S)-1-etilpirrolidin-2- il]metil}amino)metil]fenil}-1H-imidazol- 4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[1-(2,2-dimetilpropanoil)pirrolidin-3-il]amino}metil)fenil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[1-(hidroximetil)butil]amino}metil)fenil]- 1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(1,1-dióxidotetrahidro-3- tienil)amino]metil}fenil)-1H-imidazol-4-il]-L-norvalinamida;

N-[1-2-{[(1R)-1-ciclohexiletil]amino}-1,1-dimetil-2-oxoetil)-1H-imidazol-4-il]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[1,1-dimetil-2-oxo-2-(3-fenilpirrolidin-1-il)etil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(1,1-dimetil-2-{[(5-metil-2-furil)metil]amino}- 2-oxoetil)-1H-imidazol-4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[1-(metoximetil)propil]amino}-1,1-dimetil-2-oxoetil)-1H-imidazol-4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[1-(metoximetil)propil]amino}-1,1-dimetil-2-oxoetil)-1H-imidazol-4-il]-L-norvalinamida;

N-(1-{2-[(3,4-difluorobencil)amino]-1,1-dimetil-2-oxoetil}-1H-imidazol-4-il)-N-2-

[(2S)-6,8-difluoro-1,2,3,4- tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(4-fluorobencil)amino]-1,1-dimetil-2-oxoetil}-1H-imidazol-4-il)-L- norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[2-furil)etil]amino}-1,1-dimetil-2-oxoetil)- 1H-imidazol-4-il]-L-norvalinamida;

N-(1-{2-[bencil(etil)amino]-1,1-dimetil-2-oxoetil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4- tetrahidronaftalen-2-il]-L- norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(1,1-dimetil-2-{metil[2-(1H-pirazol-1- il)etil]amino}-2-oxoetil)-1H-imidazol-4- il]-L-norvalinamida;

N-[1-(2-{[(1S)-1-ciclohexiletil]amino}-1,1-dimetil-2-oxoetil)-1H-imidazol-4-il]-N-2-[(2S)-6,8-difluoro-1,2,3,4- tetrahidronaftalen-2-il]-L-norvalinamida;

N-(1-{2-[(2,4-difluorobencil)amino]-1,1-dimetil-2-oxoetil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4- tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{1,1-dimetil-2-[metil(2-piridin-2-iletil)amino]-2-oxoetil}-1H-imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(4-hidroxitetrahidro-2H-tiopiran-4-il)metil]amino}etil)-1H-imidazol-4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(2-metoxi-1-metiletil)amino]etil}-1H- imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(2-metoxi-1-metiletil)amino]etil}-1H- imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(3-etoxipropil)amino]etil}-1H-imidazol-4- il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(3-metoxipropil)amino]etil}-1H-imidazol- 4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(2-isopropoxietil)amino]etil}-1H-imidazol- 4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(2-isopropoxietil)amino]etil}-1H-imidazol-4- il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2S)-tetrahidrofuran-2-ilmetil]amino}etil)-1H-imidazol-4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2S)-tetrahidrofuran-2-ilmetil]amino}etil)-1H-imidazol-4-il]-L-norvalinamida;

N-[1-(2-{[(1R)-1-ciclohexiletil]amino}etil)-1H-imidazol-4-il]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(3-isopropoxipropil)amino]etil}-1H-imidazol-4- il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[2-(metiltio)etil]amino}etil)-1H-imidazol-4- il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(tetrahidro-2H-piran-3-ilmetil)amino]etil}-1H-imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(2R)-tetrahidrofuran-2-ilmetil]amino}etil)- 1H-imidazol-4-il]-L-norvalinamida;

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N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(2-metoxietil)amino]etil}-1H-imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-({1-[(2S)-2-hidroxibutil]pirrolidin-2-il}metil)-1H- imidazol-4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{[1-(2,2-dimetilpropil)-3-hidroxipiperidin-3- il]metil}-1H-imidazol-4-il)-L- norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-({1-[(2S)-2-hidroxibutil]pirrolidin-2-il}metil)-1H- imidazol-4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1,3-dimetilpirrolidin-3-il)metil]amino}metil)-4,5-difluorofenil]-1H-imidazol-4-il}-L-norvalinamida;

N-(1-{2-[({2-[butil(metil)amino]etil}amino)metil]-4,5-difluorofenil}-1H-imidazol-4-il)-N-2- [(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[1-(2,2-dimetilpropil)-2-oxopirrolidin-3-il]-1H- imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{(1S)-2-[(3-metoxipropil)amino]-1-metiletil}-1H- imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[(1-hidroxiciclohexil)metil]amino}carbonil)ciclobutil]-1H-imidazol-4-il}-L-norvalinamida;

N-[1-(2-{[(3,4-difluorobencil)amino]carbonil}ciclobutil)-1H-imidazol-4-il]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(2-metilbencil)amino]-2-oxoetil}-1H- imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-oxo-2-[(tetrahidro-2H-piran-2- ilmetil)amino]etil}-1H-imidazol-4-il)-L-norvalinamida;

N-(1-{2-[(3,4-difluorobencil)amino]-2-oxoetil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-[1-(2-{[(1S)-1-ciclohexiletil]amino}-2-oxoetil)-1H-imidazol-4-il]-N-2-[(2S)-6,8-difluoro-1,2,3,4- tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(4-fluorobencil)amino]-2-oxoetil}-1H- imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[2-(2-furil)etil]amino}-2-oxoetil)-1H-imidazol-4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[metil(2-piridin-2-iletil)amino]-2- oxoetil}-1H-imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(5-metil-2-furil)metil]amino}-2-oxoetil)- 1H-imidazol-4-il]-L-norvalinamida;

N-(1-{2-[(2,4-difluorobencil)amino]-2-oxoetil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-[1-(2-{[(1R)-1-ciclohexiletil]amino}-2-oxoetil)-1H-imidazol-4-il]-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-oxo-2-{[(2R)-tetrahidrofuran-2- ilmetil]amino}etil)-1H-imidazol-4-il]-L-norvalinamida;

N-(1-{2-[bencil(etil)amino]-2-oxoetil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[1-(tetrahidro-2H-piran-4-ilmetil)azetidin- 3-il]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-({(2S)-1-[(2S)-2-hidroxipropil]azetidin-2- il}metil)-1H-imidazol-4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[1-(trifluoroacetil)pirrolidin-3- il]amino}metil)fenil]-1H-imidazol-4-il}- L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[1-(2,2,2-trifluoroetil)pirrolidin-3-il]amino}metil)fenil]-1H-imidazol-4-il}- L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(3-metoxipropil)amino]-1-metil-2-oxoetil}-1H-imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(tetrahidro-2H-piran-4-ilamino)metil] fenil}-1H-imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[4-(2,2,2-trifluoroetil)piperazin-1-il]metil}fenil)-1H-imidazol-4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[4-(trifluoroacetil)piperazin-1- il]metil}fenil)-1H-imidazol-4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{(1S)-2-[(2-metoxietil)amino]-1-metiletil}-1H- imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[(1S)-1-metil-2-{metil[(1-metil-1H-pirazol-4- il)metil]amino}etil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[(1S)-1-metil-2-(5-oxo-1,4-diazepan-1-il)etil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[(1S)-1-metil-2-{metil[2-(1H-pirazol-4- il)etil]amino}etil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{(1S)-2-[(3-etoxi-2-hidroxipropil)amino]-1-metiletil}-1H-imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{(1S)-2-[(2-metoxi-1-metiletil)amino]-1- metiletil}-1H-imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[(1S)-2-{[(1S)-2-metoxi-1-metiletil]amino}-1-metiletil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[(1S)-1-metil-2-{metil[(1-metil-1H-imidazol-2-il)metil]amino}etil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[2-({[1-(trifluoroacetil)piperidin-4- il]amino}metil)fenil]-1H-imidazol-4-il}- L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(1-hidroxiciclopentil)metil]amino}-1,1-dimetil-2-oxoetil)-1H-imidazol-4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[4-(2-metoxietoxi)piperidin-1-il]-1,1-dimetil-2-oxoetil}-1H-imidazol-4-il)-L- norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(1-hidroxiciclobutil)metil]amino}-1,1-dimetil-2-oxoetil)-1H-imidazol-4-il]-L-

norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(2-hidroxi-2-fenilpropil)(metil)amino]-1,1-dimetil-2-oxoetil}-1H-imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(1-hidroxiciclopentil)metil]amino}-1-metil-2-oxoetil)-1H-imidazol-4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-[1-(2-{[(1-hidroxiciclobutil)metil]amino}-1-metil- 2-oxoetil)-1H-imidazol-4-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[(2-hidroxi-2-fenilpropil)(metil)amino]-1- metil-2-oxoetil}-1H-imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{1-metil-2-oxo-2-[(tetrahidro-1H-pirrolizin-7a(5H)-ilmetil)amino]etil}-1H-imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{2-[2-(2-hidroxietil)piperidin-1-il]-1-metil-2- oxoetil}-1H-imidazol-4-il)-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[1-({[1-(metoximetil)propil]amino}carbonil) propil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[1-({[1-(metoximetil)propil]amino}metil) propil]-1H-imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[(1S,2S)-2-{[(2-morfolin-4- iletil)amino]carbonil}ciclobutil]-1H- imidazol-4-il}-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[(1R,2R)-2-({[1-(metoximetil)propil] amino}carbonil)ciclobutil]-1H- imidazol-4-il}-L-norvalinamida;

N-{1-[(1-bencil-4-etilazetidin-2-il)metil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-{1-[1-({[(1-hidroxiciclobutil)metil]amino}carbonil) propil]-1H-imidazol-4-il}-L-norvalinamida;

N-{1-[(4-bencilmorfolin-3-il)metil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-(1-{[4-(ciclopropilmetil)morfolin-3-il]metil}-1H-imidazol-4-il)-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{1-[(dimetilamino)metil]ciclopropil}-1H-imidazol-4-il)-L-norvalinamida;

N-{1-[(4-bencilmorfolin-2-il)metil]-1H-imidazol-4-il}-N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-L-norvalinamida;

N-2-[(2S)-6,8-difluoro-1,2,3,4-tetrahidronaftalen-2-il]-N-(1-{1-[(isopropilamino)metil]ciclopropil}-1H-imidazol-4-il)-L-norvalinamida;

y las sales farmacéuticamente aceptables de los mismos.

14. Una composición farmacéutica para tratar una enfermedad o afección seleccionada entre el grupo constituido por enfermedad de Alzheimer, hemorragia cerebral hereditaria con amiloidosis, angiopatía amiloide cerebral, una enfermedad mediada por priones, miositis por cuerpos de inclusión, accidente cerebrovascular, esclerosis múltiple, trauma cefálico, alteración cognitiva suave y síndrome de Down en un mamífero que comprende una cantidad de un compuesto de acuerdo con la reivindicación 1 que es eficaz en

la inhibición de la producción de Aβ- péptidos o en el tratamiento de tal enfermedad o afección, y un vehículo farmacéuticamente aceptable.

15. Una composición farmacéutica para tratar una enfermedad o afección seleccionada entre el grupo constituido por enfermedad de Alzheimer, hemorragia cerebral hereditaria con amiloidosis, angiopatía amiloide cerebral, una enfermedad mediada por priones, miositis por cuerpos de inclusión, accidente cerebrovascular, esclerosis múltiple, trauma cefálico, alteración cognitiva suave y síndrome de Down en un mamífero que comprende una cantidad de un compuesto de acuerdo con la reivindicación 7 que es eficaz en la inhibición de la producción de Aβ- péptidos o en el tratamiento de tal enfermedad o afección, y un vehículo farmacéuticamente aceptable.

16. Un procedimiento de tratamiento de una enfermedad o afección seleccionada entre el grupo constituido por enfermedad de Alzheimer, hemorragia cerebral hereditaria con amiloidosis, angiopatía amiloide cerebral, una enfermedad mediada por priones, miositis por cuerpos de inclusión, accidente cerebrovascular, esclerosis múltiple, trauma cefálico, alteración cognitiva suave y síndrome de Down en un mamífero que comprende la administración a cada mamífero de una cantidad de un compuesto de acuerdo con la reivindicación 1 que es eficaz en la inhibición de la producción de Aβ-péptidos o en el tratamiento de tal enfermedad o afección.

17. Un procedimiento de tratamiento de una enfermedad o afección seleccionada entre el grupo constituido por enfermedad de Alzheimer,

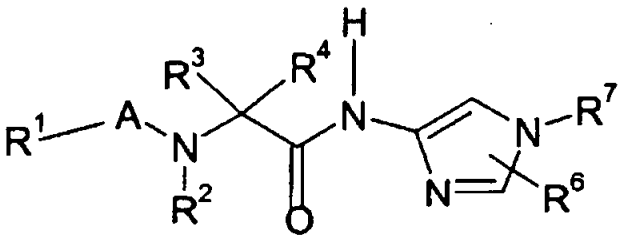
hemorragia cerebral hereditaria con amiloidosis, angiopatía amiloide cerebral, una enfermedad mediada por priones, miositis por cuerpos de inclusión, accidente cerebrovascular, esclerosis múltiple, trauma cefálico, alteración cognitiva suave y síndrome de Down en un mamífero que comprende la administración a dicho mamífero de una cantidad de un compuesto de acuerdo con la reivindicación 7 que es eficaz en la inhibición de la producción de Aβ-péptidos o en el tratamiento de tal enfermedad o afección.

18. Una composición farmacéutica para tratar una enfermedad o afección asociada a la modulación de la ruta de señalización de Notch que comprende el compuesto de fórmula I de acuerdo con la reivindicación 1, o sus sales farmacéuticamente aceptables.

19. Una composición farmacéutica para tratar una enfermedad o afección asociada a la modulación de la ruta de señalización de Notch que comprende el compuesto de fórmula I de acuerdo con la reivindicación 1, o sus sales farmacéuticamente aceptables.

Resumen de la invención

La presente invención se refiere a los compuestos de fórmula I



I

en la que R^1, R^2, R^3, R^4, R^6, R^7, y A son como se han definido. Los compuestos de la fórmula I tienen actividad en la inhibición de la producción de Aβ-péptidos. La invención también se refiere a las composiciones farmacéuticas y procedimientos para tratar enfermedades y trastornos, por ejemplo, trastornos neurodegenerativos y/o neurológicos, por ejemplo enfermedad de Alzheimer, en un mamífero que comprende los compuestos de la fórmula I.

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB2006/002753	11.09.2006	22.09.2005

International Patent Classification (IPC) or both national classification and IPC
INV. C07D233/54 C07D401/04 C07D403/04 C07D403/10 C07D403/12 C07D401/12 C07D405/12 C07D405/06 C07D401/06 C07D409/12 C07D413/12 C07D487/04 C07D487/08 A61K31/4178

Applicant
PFIZER PRODUCTS INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ 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 Rule 43*bis*.1(a)(i) 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

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	see form PCT/ISA/210	Jeanjean, Fabien Telephone No. +49 89 2399-2920

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IB2006/002753

A30

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material:

      ☐ on paper

      ☐ in electronic form

   c. time of filing/furnishing:

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in electronic form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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. 1-11 (all in-part), 13-19 (all in-part), 16-17 (industrial applicability)

because:

☒ the said international application, or the said claims Nos. 16-17 (industrial applicability) relate to the following subject matter which does not require an international search *(specify)*:

see separate sheet

☐ 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 *(specify)*:

☒ no international search report has been established for the whole application or for said claims Nos. 1-11 (all in-part), 13-19 (all in-part)

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic 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

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:

   ☐ paid additional fees

   ☐ paid additional fees under protest and, where applicable, the protest fee

   ☐ paid additional fees under protest but the applicable protest fee was not paid

   ☒ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-11 (all in-part), 12, 13-19 (all in-part)

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-11 (all in-part), 12, 13-19 (all in-part)
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-11 (all in-part), 12, 13-19 (all in-part)
Industrial applicability (IA)	Yes:	Claims	1-11 (all in-part), 12, 13-15 (all in-part), 18-19 (all in-part)
	No:	Claims	

2. Citations and explanations

   see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

   and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

see form 210

Re Item III.

Claims 16 and 17 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Only the claims 1 to 11 (all in-part), 12 and 13-19 (all in-part) have been searched since the application lacks unity (see Item IV).

Re Item IV.

This Authority considers that there are 3 inventions covered by the claims indicated as follows:

I: Claims 1 to 11 (all in-part), 12, 13-19 (all in-part) related to the compounds of formula I and their compositions wherein A is absent.
II: Claims 1 to 11 and 13-19 (all in-part) related to the compounds of formula I and their compositions wherein A is -CO-, -NR^9-CO-, -Z-CO-.
III: Claims 1 to 11 and 13-19 (all in-part) related to the compounds of formula I and their compositions wherein A is -Z-CS- and SO_2.

The reasons for which the inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT, are as follows:

The closest prior art for the present application is represented by D1 relating to compositions comprising a Growth hormonesecretagogue (GHS) and a kinase inhibitor acting synergistically in promoting the clearance of Aβ from the brain and therefore useful for retarding, arresting or preventing the accumulation of Aβ in the brain (p. 5, l. 4 and 5). D1 discloses compound VII (p. 11, l. 1 to 5). The known compound of D1 differs from the compound of formula I of claim 1 of the present application in that the phenyl and the amino groups are not encompassed by the formula I.

The technical problem underlying the present claims is seen in the provision of alternative compounds useful for treating diseases associated with the deposition of β-amyloid in the brain, such as Alzheimer's disease.

The common structural feature shared by all the alternatives of the application is seen as a N-(*1H*-imidazol-4-yl)-2-amino-acetamide. This structural feature is already known from D1. Furthermore these alternatives do not belong to a recognised class of chemical compounds which are expected to behave in the same way in the context of the claimed invention.
The three inventions do not share a common special technical feature as required by rule 13.2 PCT. Therefore the application lacks unity of invention (Rule 13.1 PCT).

● Only the first invention has been searched.

D1 = WO2005058308

Re Item V.
Reasoned statement with regard to novelty, inventive step or industrial applicability of the first invention; citations and explanations supporting such statement

1 Reference is made to the following documents:

● D1 = WO2005058308
D2 = WO0210141

2 Novelty

2.1 The subject-matter of the first invention seems to be new in the sense of Article 33(2) PCT.

2.2 The document D1 discloses (the references in parentheses applying to this document): compound VII (p. 11, l. 1 to 5). The known compound of D1 differs from the compound of formula I of claim 1 of the present application in that the phenyl and the amino groups are not encompassed by the formula I.
Novelty is acknowledged for the first invention vis-à-vis D1.

2.3 The document D2 discloses (the references in parentheses applying to this document): a compound of formula 1 (p. 61, cl. 1, l. 1 to 5), wherein R^3 may be -$C(O)(CR^{10}R^{11})_n$, n may be 0, R^4 may be C1 and may be substituted by -NR^7R^8. D2 discloses the specific compound of example 2 (p. 48, l. 30 and 31). There is an overlapping between this formula and the formula I wherein A is absent of the present application. At the light of the example 2 of D2, there is one new technical element provided by the present application establishing a new technical teaching. An amino group takes place of the phenyl and the nitrogen has to be substituted which is not specified in D2.
Novelty is acknowledged for the first invention vis-à-vis D2.

3 Inventive step

3.1 The subject-matter of the first invention does not involve an inventive step in the sense of Article 33(3) PCT.

3.2 The document D2 is regarded as being the closest prior art to the subject-matter of the first invention, and discloses (the references in parentheses applying to this document): a compound of formula 1 (p. 61, cl. 1, l. 1 to 5), wherein R^3 may be -$C(O)(CR^{10}R^{11})_n$, n may be 0, R^4 may be C1 and may be substituted by -NR^7R^8. There is an overlapping between this formula and the formula I wherein A is absent of the present application. The compounds of D2 are useful for treating a neurodegenerative disease (p. 64, cl. 10, l. 23 to 25) such as Alzheimer's disease (p. 13, l. 10 to 12).
The skilled reader knows that mere reproduction of the compounds described in D2 would lead to compounds retaining the claimed activity. The provision of alternatives compounds for the treatment of neurodegenerative diseases is thus solved in a obvious way by the skilled reader.

The problem underlying the current application appears to be the provision of further compounds having unexpected properties over the prior art.
On the basis of the content of the description, this problem has not yet been solved.
An inventive step cannot therefore be acknowledged for the subject-matter of the first invention.

Remarks

1 Claims 18 and 19 refer to a mechanism and not to a specific disease which render unclear claims 18 and 19.

2 The drawing of example 206 does not comply with the given formula.

3 Some examples (see for instance examples 173 to 188) do not fall within the scope of formula I of claim 1 of the present invention (difference at R^7). This inconsistency between the description and the claim 1 render claim 1 unclear.

4 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1 and D2 is not mentioned in the description, nor are these documents identified therein.

Re Item V.

US20050215610: Pub. Date: 29th September 2005
WO2005092864: Pub. Date: 6th October 2005
The patents US20050215610 and WO2005092864 have been published after the priority date of the present application. According to rule 64.3 PCT these documents may not be taken into account for the assessment of novelty and inventive step during the international phase.These documents could be relevant if the application would enter in the European phase.

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
29 March 2007 (29.03.2007)

PCT

(10) International Publication Number
WO 2007/034326 A3

(51) International Patent Classification:
C07D 233/54 (2006.01) *C07D 405/06* (2006.01)
C07D 401/04 (2006.01) *C07D 401/06* (2006.01)
C07D 403/04 (2006.01) *C07D 409/12* (2006.01)
C07D 403/10 (2006.01) *C07D 413/12* (2006.01)
C07D 403/12 (2006.01) *C07D 487/04* (2006.01)
C07D 401/12 (2006.01) *C07D 487/08* (2006.01)
C07D 405/12 (2006.01) *A61K 31/4178* (2006.01)

(21) International Application Number:
PCT/IB2006/002753

(22) International Filing Date:
11 September 2006 (11.09.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/719,521 22 September 2005 (22.09.2005) US

(71) Applicant *(for all designated States except US)*: **PFIZER PRODUCTS INC.** [US/US]; Eastern Point Road, Groton, CT 06340 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **BRODNEY, Michael, Aaron** [US/US]; Pfizer Global Research and Development, Eastern Point Road, Groton, CT 06340 (US). **CHEN, Yuhpyng, Liang** [US/US]; Pfizer Global Research and Development, Eastern Point Road, Groton, CT 06340 (US). **COFFMAN, Karen, Jean** [US/US]; Pfizer Global Research and Development, Eastern Point Road, Groton, CT 06340 (US). **KLEINMAN, Edward, Fox** [US/US]; Pfizer Global Research and Development, Eastern Point Road, Groton, CT 06340 (US). **O'NEILL, Brian, Thomas** [US/US]; Pfizer Global Research and Development, Eastern Point Road, Groton, CT 06340 (US).

(74) Agent: **FULLER, Grover, F., Jr.**; c/o LAWRENCE, Jackie, Pfizer Inc. MS8260-1615, Eastern Point Road, Groton, CT 06340 (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, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

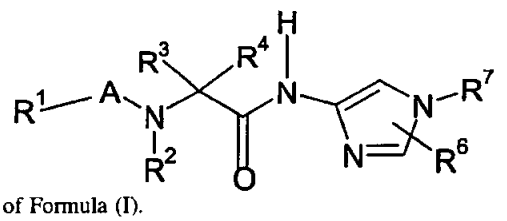
(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT,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

Published:
— *with international search report*

(88) Date of publication of the international search report:
30 August 2007

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: IMIDAZOLE COMPOUNDS FOR THE TREATMENT OF NEUROLOGICAL DISORDERS



(I)

of Formula (I).

(57) Abstract: The present invention relates to compounds of Formula (I) wherein R^1, R^2, R^3, R^4, R^6, R^7 and A are as defined. Compounds of Formula (I) have activity inhibiting production of Aβ-peptide. The invention also relates to pharmaceutical compositions and methods for treating diseases and disorders, for example, neurodegenerative and/or neurological disorders, e.g., Alzheimer's disease, in a mammal comprising compounds

WO 2007/034326 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2006/002753

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D233/54 C07D401/04 C07D403/04 C07D403/10 C07D403/12
C07D401/12 C07D405/12 C07D405/06 C07D401/06 C07D409/12
C07D413/12 C07D487/04 C07D487/08 A61K31/4178

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)
C07D A61K

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 practical, search terms used)
EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2005/058308 A2 (MERCK SHARP & DOHME [GB]; CASTRO PINEIRO JOSE LUIS [GB]) 30 June 2005 (2005-06-30) page 5, lines 4,5 page 11, lines 1-5; compound VII	1-19
X	WO 02/10141 A (PFIZER PROD INC [US]; AHLIJANIAN MICHAEL KIRK [US]; COOPER CHRISTOPHER) 7 February 2002 (2002-02-07) page 13, lines 10-12 page 48, lines 30,31; example 2 page 61, lines 1-5; claim 1 page 64, lines 23-25; claim 10	1-19
P,X	WO 2005/092864 A (PFIZER PROD INC [US]; BRODNEY MICHAEL AARON [US]; COFFMAN KAREN JEAN [) 6 October 2005 (2005-10-06) page 86; claim 1	1-19

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[X] Further documents are listed in the continuation of Box C.

[X] 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 document but 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
23 February 2007	21/05/2007

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Jeanjean, Fabien

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2006/002753

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	US 2005/215610 A1 (BRODNEY MICHAEL A [US] ET AL) 29 September 2005 (2005-09-29) page 41; claim 1	1-19

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2006/002753

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see annex

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

International Application No. PCT/IB2006 /002753

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-11 (all in-part), 12, 13-19 (all in-part)

   related to the compounds of formula I and their compositions wherein A is absent.

   ---

2. claims: 1-11 and 13-19 (all in-part)

   related to the compounds of formula I and their compositions wherein A is -CO-, -NR9-CO-, -Z-CO-

   ---

3. claims: 1-11 and 13-19 (all in-part)

   related to the compounds of formula I and their compositions wherein A is -Z-CS- and SO2

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2006/002753

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2005058308 A2	30-06-2005	NONE	
WO 0210141 A	07-02-2002	AR 032629 A1	19-11-2003
		AU 7094401 A	13-02-2002
		BG 107469 A	30-09-2003
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		HR 20030048 A2	30-04-2003
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		ZA 200300819 A	20-04-2004
WO 2005092864 A	06-10-2005	AR 049875 A1	13-09-2006
		AU 2005225635 A1	06-10-2005
		CA 2560580 A1	06-10-2005
		CN 1934091 A	21-03-2007
		EP 1730119 A1	13-12-2006
		KR 20060123651 A	01-12-2006
		NL 1028598 C2	03-01-2006
		NL 1028598 A1	26-09-2005
US 2005215610 A1	29-09-2005	NONE	

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

No 08 024630 00000 0000

Fecha 2008 03 07 16 56 05 Dep 2020 NUECREACIONI
Tra 11 PATENTEIYII Eve 378 FASENACIONALI
Act 411 PRESENTACION Folios 440

Industria y Comercio
SUPERINTENDENCIA

REQUISITOS MINIMOS PARA ADMISION A TRAMITE PCT

PATENTE DE INVENCION [✓] MODELO DE UTILIDAD [ ]

- Indicación de que se solicita la concesión de una patente [✓]
- Datos de identificación del solicitante o de la persona que 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 y 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 se 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 trazado [ ]
- Comprobante de pago de las tasas establecidas [ ]

COMPLETA [ ] INCOMPLETA [ ]

Firma Responsable

Fecha_____

Carrera 13 No 27-00 Piso 5, 7 y 10
Conmutador 3 82 08 40
Fax 350 62 20
E-mail info@sic.gov.co
www sic gov co
Bogotá, D C , Colombia

REPUBLICA DE COLOMBIA
SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

Folio 442

2020
Bogotá D.C.,

Doctor(a)
OLARTE GARCIA CARLOS REINALDO
Apoderado(a) y/o Representante de
PFIZER PRODUCTS INC.

REFERENCIA	Radicación No.	8 24630
	Solicitud internacional	PCT/IB2006/002753
	Fecha inicio fase nacional	22/04/2008
	Trámite	11
	Evento	378
	Actuación	416
	Oficio No.	5935
	Folios	1

Teniendo en cuenta que la solicitud de privilegio de patente que se tramita bajo el expediente indicado en la referencia, reúne los requisitos de forma establecidos en la Decisión 486 de la Comisión de la Comunidad Andina, el Tratado de Cooperación en Materia de Patentes (PCT), el Reglamento y la Circular Única de la Superintendencia de Industria y Comercio, se envía el extracto de la solicitud a la Oficina de Comunicaciones para efecto de su publicación en la Gaceta de Propiedad Industrial.

Cúmplase
Dado en Bogotá D.C., 13 MAY 2008

ALIX CARMENZA CESPEDES DE VERGEL
Jefe de la división de Nuevas Creaciones

adpa11

Industria y Comercio
SUPERINTENDENCIA

DIVISIÓN DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No.08-024630

EL EXTRACTO DE LA PRESENTE SOLICITUD DE **PATENTE DE INVENCIÓN**

FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No **593** DE

FECHA **27** DE **JUNIO DE 2008** EL TÉRMINO HÁBIL SEÑALADO POR LA LEY

EXPIRA EL **13** DE **ENERO** DEL **2009**

NOTA: Dentro del plazo de los seis (6) meses siguientes a partir de la fecha de publicación en la gaceta de Propiedad Industrial, deberá solicitar y cancelar el examen de patentabilidad so pena de que la solicitud caiga en abandono, de acuerdo con lo establecido en el Artículo 44 de la Decisión 486/2000.

SE PRESENTARON OPOSICIONES POR PARTE DE TERCEROS.

SI __ _____ NO__ ___ **X** _____