Industria y Com
SUPERINTENDENCIA

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
No. 12-040232- -00000-0000
Fecha: 2012-03-07 16:43:07 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 411 PRESENTACION Folios: 1165

DELEGATURA DE PROPIEDAD INDUSTRIAL

División de Nuevas Creaciones

SOLICITUD

PATENTE DE INVENCIÓN

21. **EXPEDIENTE No.** _____

54. **TÍTULO** QUINAZOLINAS COMO INHIBIDORES DE LOS CANALES IONICOS DE POTASIO

51. **CLASIFICACIÓN INTERNACIONAL** _____

71. **SOLICITANTE** BRISTOL-MYERS SQUIBB COMPANY

DOMICILIO PRINCETON, NEW JERSEY, ESTADOS UNIDOS

74. **APODERADO** ALVARO CORREA ORDOÑEZ

22. **BOGOTÁ, D. C.,** MARZO 06, 2012

(FORMA P-10)

115198-Imprenta Nacional de Colombia-2011

PETITORIO

Industria y Comercio
SUPERINTENDENCIA

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
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Act. 411 PRESENTACION Folios: 1165

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FORMULARIO ÚNICO DE SU

PCT

ENTRADA EN FASE NACIONAL

(1) **SOLICITUD DE :**

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

[X] Capítulo I. [ ] Capítulo II.

(2) **SOLICITANTE** (71)	Nombre: **BRISTOL-MYERS SQUIBB COMPANY** Dirección: Route 206 and Province Line Road Princeton, New Jersey 08543-4000, U.S.A. Nacionalidad o Domicilio: Estados Unidos de América Lugar de Constitución: Estados Unidos de América Teléfono: Fax: E-Mail	**IDENTIFICACION** C.C. [ ] NIT [ ] C.E. [ ] Otro [ ] Cual Número
(3) **REPRESENTANTE O APODERADO**	Nombre: ALVARO CORREA ORDOÑEZ Dirección: Avenida 82 No. 10-62 Piso 6 Teléfono: 6341500 Fax: 3762211 E-Mail: office.bogota@bakermckenzie.com	**IDENTIFICACION** C.C. [X] NIT [ ] C.E. [ ] Otro [ ] Cual Número 79.143.366 Usaquén TP 20281
(4) **INVENTOR (ES)** (72)	Nombre: JOHNSON, James A.; LLOYD, John; FINLAY, Heather; JIANG, Ji; NEELS, James; DHONDI, Naveen Kumar; GUNAGA, Prashantha; BANERJEE, Abhisek; ADISECHAN, Ashokkumar Dirección: c/o Bristol-Myers Squibb Company 311 Pennington-Rocky Hill Road Pennington, New Jersey 08534 (US); c/o Bristol-Myers Squibb Company 311 Pennington-Rocky Hill Road Pennington, New Jersey 08534 (US); c/o Bristol-Myers Squibb Company 311 Pennington-Rocky Hill Road Pennington, New Jersey 08534 (US); c/o Bristol-Myers Squibb Company 311 Pennington-Rocky Hill Road Pennington, New Jersey 08534 (US); c/o Bristol-Myers Squibb Company Route 206 and Province Line Road Princeton, New Jersey 08543 (US); House No. 5-6-286 Kakatiyanagar Colony Kamareddy Andra Pradesh 503111 (IN); 286 Royal Lake Front Residency Jambu Savari Dinne Bangalore 560076 (IN); B/1, Kali Banerjee Lane Howrah West Bengal 711101 (IN); 17B(a), Hudco House Thally Road Hosur Tamil Nadu 635109 (IN) Nacionalidad o Domicilio: Estados unidos de América e India (Respectivamente)	

(5) **PCT (85)**

Solicitud Internacional No.	PCT/US2010/047430	Fecha	01-09-2010
Publicación Internacional No.	WO 2011/028741	Fecha	10-03-2011

(6) **Título (54)** QUINAZOLINAS COMO INHIBIDORES DE LOS CANALES IONICOS DE POTASIO

(7) **Clasificación Internacional (51)** C07D 239/95; C07D 401/12; C07D 401/14; C07D 403/04; C07D 403/12; C07D 407/12; C07D 413/14; C07D 417/12; C07D 417/14; *A61K 31/517*

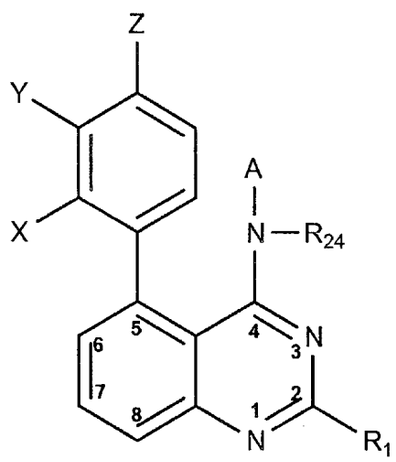
(8) **Prioridad**	(33) País de Origen	(32) Fecha	(31) Número de Solicitud
SI [X] NO [ ]	US	03-09-2009	61/239,452

(9) **Comprobante de pago No.** 12-0021409 – 12-008924 – 12-0015554 **Fecha** 29-02-12 – 30-01-12 – 15-02-12

(10) **ANEXOS**

- [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
- [X] Documento de cesión del inventor al solicitante o a su causante
- [X] 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: Extractos

(11) **FIGURA CARATERISTICA**



(I)

(12) Solicito la concesión de la patente,

NOMBRE: ALVARO CORREA ORDOÑEZ

FIRMA:

C.C. 79.143.366 de Usaquén T.P. 20.281

Instrucciones para la presentación de los anexos, ver reverso de esta página

RECIBO DE PAGO

3

30121005

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
NIT : 800.176.089-2
- / -

Industria y Comercio
SUPERINTENDENCIA

RECIBO DE CAJA

No. 12 - 0021409

Bogotá D.C., Febrero 29 de 2012 - 16:46:18

RECIBIDO DE : BAKER & MCKENZIE NI 900.034.906

*** Soporte del Pago ***

TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PAGO	VR.PAGO
CONSIGNACION	BANCO DE BOGOTA	062754387	411692632	28/02/2012	62.480.000.00

*** Conceptos Pagados ***

CANT.	RENTISTICO	CONCEPTO	Vr.UNDITARIO	Vr.CONCEPTO
1	50005-01-01 SOLICITUDES	1 TRAMITES DE SOL. DE PATENTE DE INVENCION	590.000.00	590.000.00
				$590.000.00

SON: **QUINIENTOS NOVENTA MIL PESOS MONEDA CORRIENTE***

Responsable: _____
-******-

Recibo de Caja Aplicado al Expediente No. _____

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
No. 12-040232- -00000-0000
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2012/002

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
NIT : 800.176.089-2
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Industria y Comercio
SUPERINTENDENCIA

RECIBO DE CAJA

No. 12 - 008934

Bogotá D.C., Enero 30 de 2012 - 16:34:29

RECIBIDO DE : BAKER & MCKENZIE NI 900.034.906

*** Soporte del Pago ***

TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PAGO	VR.PAGO
CONSIGNACION	BANCO DE BOGOTA	062754387	450325595	27/01/2012	83.977.500.00

*** Conceptos Pagados ***

CANT.	RENTISTICO	CONCEPTO	Vr.UNDITARIO	Vr.CONCEPTO
1	50005-01-09 OTROS SERVICIOS DE PROPIEDAD INDUSTRIAL	54 INFORMACION DETALLADA DE UN TRAMITE	30.000.00	30.000.00
				$30.000.00

SON: **TREINTA MIL PESOS MONEDA CORRIENTE***

Responsable: _____
-****-

Recibo de Caja Aplicado al Expediente No. _____

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
No. 12-040232- -00000-0000
Fecha: 2012-03-07 16:43:07 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 411 PRESENTACION Folios: 1165

2012/003

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
NIT : 800.176.089-2
- / -

Industria y Comercio
SUPERINTENDENCIA

RECIBO DE CAJA

No. 12 - 0015554

Bogotá D.C., Febrero 15 de 2012 - 16:59:30

RECIBIDO DE : BAKER & MCKENZIE NI 900.034.906

*** Soporte del Pago ***

TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PAGO	VR.PAGO
CONSIGNACION	BANCO DE BOGOTA	062754387	325085342	14/02/2012	98.870.000.00

*** Conceptos Pagados ***

CANT.	RENTISTICO	CONCEPTO	Vr.UNDITARIO	Vr.CONCEPTO
1	50005-01-03	CAMBIO DE MODALIDAD Y MODIFICACIONES NEG N.CREACION CORRECCION A SOLICITUD EN TRAMITE / MODOFICA	120.000.00	120.000.00
				$120.000.00

SON: **CIENTO VEINTE MIL PESOS MONEDA CORRIENTE***

Responsable: _____

Recibo de Caja Aplicado al Expediente No. _____

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
No. 12-040232- -00000-0000
Fecha: 2012-03-07 16:43:07 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
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EXTRACTOS

Industria y Comercio
SUPERINTENDENCIA

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES
TARJETA ARCHIVO PROPIETARIOS

SUPERINTENDENCIA PATENTE DE INVENCION ____ PCT X MODELO DE UTILIDAD ____ DISEÑO INDUSTRIAL ___

(21) N° de solicitud: (22) Fecha de solicitud:

(51) Clasificación Internacional: C07D 239/95; C07D 401/12; C07D 401/14; C07D 403/04; C07D 403/12; C07D 407/12; C07D 413/14; C07D 417/12; C07D 417/14; *A61K 31/517*

(71) Solicitante(s): **BRISTOL-MYERS SQUIBB COMPANY**

(72) Inventor(es): JOHNSON, James A.; LLOYD, John; FINLAY, Heather; JIANG, Ji; NEELS, James; DHONDI, Naveen Kumar; GUNAGA, Prashantha; BANERJEE, Abhisek; ADISECHAN, Ashokkumar

(30) Prioridad	(31) ***No. Prioridad***	32) ***Fecha***	(33) ***País***
	61/239,452	03-09-2009	US

(85) Fecha inicio fase nacional: 03-04-2012

(86) Datos relativos a la presentación de la solicitud PCT
Fecha de presentación de la solicitud: 01-09-2010
No. de solicitud: PCT/US2010/047430

(87) Publicación internacional
Fecha: 10-03-2011
N° publicación: WO 2011/028741

(54) Titulo: QUINAZOLINAS COMO INHIBIDORES DE LOS CANALES IONICOS DE POTASIO

Industria y Comercio
SUPERINTENDENCIA

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES
TARJETA ARCHIVO TEMATICO

SUPERINTENDENCIA PATENTE DE INVENCION ___ PCT _X_ MODELO DE UTILIDAD ___ DISEÑO INDUSTRIAL ___

(21) N° de solicitud: (22) Fecha de solicitud:

(51) Clasificación Internacional: C07D 239/95; C07D 401/12; C07D 401/14; C07D 403/04; C07D 403/12; C07D 407/12; C07D 413/14; C07D 417/12; C07D 417/14; *A61K 31/517*

(71) Solicitante(s) **BRISTOL-MYERS SQUIBB COMPANY**

(72) Inventor(es): JOHNSON, James A.; LLOYD, John; FINLAY, Heather; JIANG, Ji; NEELS, James; DHONDI, Naveen Kumar; GUNAGA, Prashantha; BANERJEE, Abhisek; ADISECHAN, Ashokkumar

(74) Apoderado: ALVARO CORREA ORDOÑEZ

(30) Prioridad	(31) ***No. Prioridad***	32) ***Fecha***	(33) ***País***
	61/239,452	03-09-2009	US

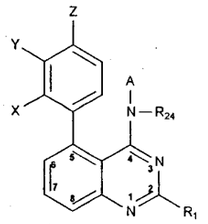
(85) Fecha límite inicio fase nacional: 03-04-2012

(86) Datos relativos a la presentación de la solic. PCT
Fecha de presentación de la solicitud 01-09-2010
No. de solicitud: PCT/US2010/047430

(87) Publicación internacional:
Fecha: 10-03-2011
No. Publicación: WO 2011/028741

(54) Titulo: QUINAZOLINAS COMO INHIBIDORES DE LOS CANALES IONICOS DE POTASIO

(57) Resumen: Un compuesto de fórmula I



CONTINUA AL RESPALDO ...

Industria y Comercio
SUPERINTENDENCIA

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES
EXTRACTO PARA PUBLICACIÓN
SOLICITUD DE PATENTE DE INVENCIÓN PCT

(21) N° de solicitud:

22) Fecha de solicitud:

(30) Prioridad (31) ***No.*** 32) ***Fecha*** (33) ***País***

61/239,452 03-09-2009 US

(51) Int Cl: C07D 239/95; C07D 401/12; C07D 401/14; C07D 403/04; C07D 403/12; C07D 407/12; C07D 413/14; C07D 417/12; C07D 417/14; *A61K 31/517*

(71)Solicitante(s) **BRISTOL-MYERS SQUIBB COMPANY**

(72)Inventor(es): JOHNSON, James A.; LLOYD, John; FINLAY, Heather; JIANG, Ji; NEELS, James; DHONDI, Naveen Kumar; GUNAGA, Prashantha; BANERJEE, Abhisek; JADISECHAN, Ashokkumar

(74) Apoderado: **ALVARO CORREA ORDOÑEZ**

(85) Fecha limite inicio fase nacional: 03-04-2012

(86) Datos relativos a la presentación de la solicitud PCT

Fecha de presentación de la solicitud: 01-09-2010

No. de solicitud PCT/US2010/047430

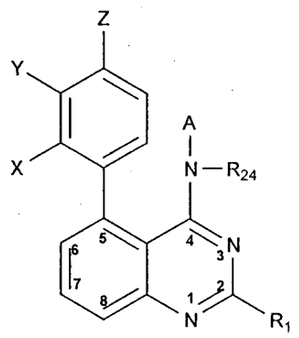
(87) Publicación internacional

Fecha: 10-03-2011

N° publicación: WO 2011/028741

(54) Titulo: QUINAZOLINAS COMO INHIBIDORES DE LOS CANALES IONICOS DE POTASIO

Resumen: Un compuesto de fórmula I



en la que A, X, Y, Z, R_1 y R_{24} se describen en el presente documento. Los compuestos son útiles como inhibidores de la función de los canales de potasio y en el tratamiento y prevención de arritmia, trastornos asociados con I_{Kur} y otros trastornos mediados por la función de los canales iónicos.

COPIA SOLICITUD
INTERNACIONAL

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
10 March 2011 (10.03.2011)

PCT

(10) International Publication Number
WO 2011/028741 A1

(51) International Patent Classification:
C07D 239/95 (2006.01) *C07D 407/12* (2006.01)
C07D 401/12 (2006.01) *C07D 413/14* (2006.01)
C07D 401/14 (2006.01) *C07D 417/12* (2006.01)
C07D 403/04 (2006.01) *C07D 417/14* (2006.01)
C07D 403/12 (2006.01) *A61K 31/517* (2006.01)

(21) International Application Number:
PCT/US2010/047430

(22) International Filing Date:
1 September 2010 (01.09.2010)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/239,452 3 September 2009 (03.09.2009) US

(71) Applicant *(for all designated States except US)*: **BRISTOL-MYERS SQUIBB COMPANY** [US/US]; P.O. Box 4000, Route 206 and ProvinceLine Road, Princeton, New Jersey 08543-4000 (US).

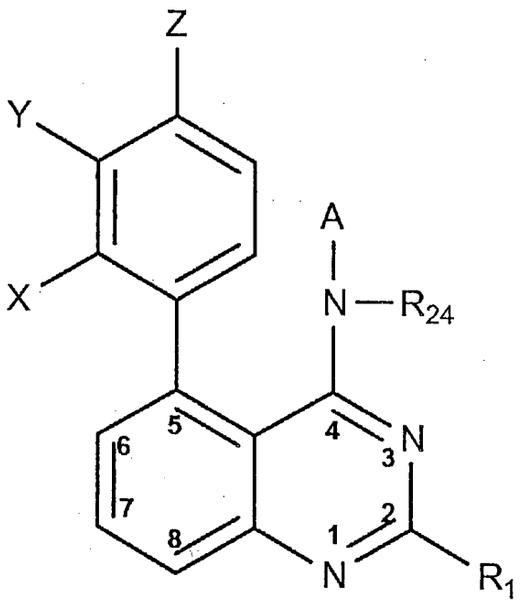
(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **JOHNSON, James A.** [US/US]; c/o Bristol-Myers Squibb Company, 311 Pennington-Rocky Hill Road, Pennington, New Jersey 08534 (US). **LLOYD, John** [US/US]; c/o Bristol-Myers Squibb Company, 311 Pennington-Rocky Hill Road, Pennington, New Jersey 08534 (US). **FINLAY, Heather** [GB/US]; c/o Bristol-Myers Squibb Company, 311 Pennington-Rocky Hill Road, Pennington, New Jersey 08534 (US). **JIANG, Ji** [CN/US]; c/o Bristol-Myers Squibb Company, 311 Pennington-Rocky Hill Road, Pennington, New Jersey 08534 (US). **NEELS, James** [US/US]; c/o Bristol-Myers Squibb Company, Route 206 and Province Line Road, Princeton, New Jersey 08543 (US). **DHONDI, Naveen Kumar** [IN/IN]; House No. 5-6-286, Kakatiyanagar Colony, Kamareddy, Andra Pradesh 503111 (IN). **GUNAGA, Prashantha** [IN/IN]; 286 Royal Lake Front Residency, Jambu Savari Dinne, Bangalore 560076 (IN). **BANERJEE, Abhisek** [IN/IN]; B/1, Kali Banerjee Lane, Howrah, West Bengal 711101 (IN). **ADISECHAN, Ashokkumar** [IN/IN]; 17B(a), Hudco House, Thally Road, Hosur, Tamil Nadu 635109 (IN).

(74) Agents: **BOGIE, Terence J.** et al.; Bristol-Myers Squibb Company, P.O. Box 4000, Princeton, New Jersey 08543-4000 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,

[Continued on next page]

(54) Title: QUINAZOLINES AS POTASSIUM ION CHANNEL INHIBITORS



(I)

(57) Abstract: A compound of formula (I) wherein A, X, Y, Z, R_1 and R_{24} are described herein. The compounds are useful as inhibitors of potassium channel function and in the treatment and prevention of arrhythmia, I_{Kur}-associated disorders, and other disorders mediated by ion channel function.

WO 2011/028741 A1

WO 2011/028741 A1

ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, 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, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

— *of inventorship (Rule 4.17(iv))*

Published:

— *with international search report (Art. 21(3))*

QUINAZOLINES AS POTASSIUM ION CHANNEL INHIBITORS

RELATED APPLICATION

[0001] This application claims the benefit of U.S. Provisional Application No. 61/239,452, filed on September 3, 2009, incorporated herein by reference in its entirety.

FIELD OF THE INVENTION

[0002] The present invention provides for quinazolines useful as inhibitors of potassium channel function (especially inhibitors of the K_v1 subfamily of voltage gated K^+ channels, more especially inhibitors of $K_v1.5$ (which have been linked to the ultra-rapidly activating delayed rectifier K^+ current I_{Kur}), and/or $K_v1.3$ channels, and/or $K_v1.1$ channels) and to pharmaceutical compositions containing such compounds. The present invention further provides for methods of using such compounds in the treatment and prevention of arrhythmia, I_{Kur}-associated disorders, and other disorders mediated by ion channel function.

BACKGROUND OF THE INVENTION

[0003] The ultra-rapidly activating delayed rectifier K^+ current (I_{Kur}) is believed to represent the native counterpart to a cloned potassium channel designated $K_v1.5$ and, while present in human atrium, it appears to be absent in human ventricle. Furthermore, because of its rapidity of activation and limited slow inactivation, I_{Kur} is believed to contribute significantly to repolarization in human atrium. Consequently, a specific blocker of I_{Kur}, that is a compound which blocks $K_v1.5$, would overcome the short coming of other compounds by prolonging refractoriness by retarding repolarization in the human atrium without causing the delays in ventricular repolarization that underlie arrhythmogenic after depolarizations and acquired long QT syndrome observed during treatment with current Class III antiarrhythmic agents. (Antiarrhythmic agents of Class III are drugs that cause a selective prolongation of the duration of the action potential without significant cardiac depression.)

[0004] Immunoregulatory abnormalities have been shown to exist in a wide variety of autoimmune and chronic inflammatory diseases, including systemic lupus erythematosis, chronic rheumatoid arthritis, type I and II diabetes mellitus,

inflammatory bowel disease, biliary cirrhosis, uveitis, multiple sclerosis and other disorders such as Crohn's disease, ulcerative colitis, bullous pemphigoid, sarcoidosis, psoriasis, ichthyosis, Graves ophthalmopathy and asthma. Although the underlying pathogenesis of each of these conditions may vary, they have in common the appearance of a variety of auto-antibodies and self-reactive lymphocytes. Such self-reactivity may be due, in part, to a loss of the homeostatic controls under which the normal immune system operates. Similarly, following a bone-marrow or an organ transplantation, lymphocytes recognize the foreign tissue antigens and begin to produce immune mediators which lead to graft rejection or graft-vs-host rejection.

[0005] One end result of an autoimmune or a rejection process is tissue destruction caused by inflammatory cells and the mediators they release. Anti-inflammatory agents such as NSAIDs act principally by blocking the effect or secretion of these mediators but do nothing to modify the immunologic basis of the disease. On the other hand, cytotoxic agents, such as cyclophosphamide, act in such a nonspecific fashion in which both the normal and autoimmune responses are shut off. Indeed, patients treated with such nonspecific immunosuppressive agents are as likely to succumb to infection as they are to their autoimmune disease.

[0006] Cyclosporin A, which was approved by the US FDA in 1983 is currently the leading drug used to prevent rejection of transplanted organs. In 1993, FK-506 (PROGRAF®) was approved by the US FDA for the prevention of rejection in liver transplantation. Cyclosporin A and FK-506 act by inhibiting the body's immune system from mobilizing its vast arsenal of natural protecting agents to reject the transplant's foreign protein. In 1994, Cyclosporin A was approved by the US FDA for the treatment of severe psoriasis and has been approved by European regulatory agencies for the treatment of atopic dermatitis. Though these agents are effective in fighting transplant rejection, Cyclosporin A and FK-506 are known to cause several undesirable side effects including nephrotoxicity, neurotoxicity, and gastrointestinal discomfort. Therefore, a selective immunosuppressant without these side effects still remains to be developed. Potassium channel inhibitors as described here promise to be the solution to this problem, since inhibitors of $K_v1.3$, for example, are immunosuppressive. See Wulff et al., "Potassium channels as therapeutic targets for autoimmune disorders," *Curr. Opin. Drug Discov. Devel.*, 6(5):640-647 (Sep. 2003);

Shah et al., "Immunosuppressive effects of a $K_v1.3$ inhibitor," *Cell Immunol.*, 221(2):100-106 (Feb. 2003); Hanson et al., "UK-78,282, a novel piperidine compound that potently blocks the $K_v1.3$ voltage-gated potassium channel and inhibits human T cell activation," *Br. J. Pharmacol.*, 126(8):1707-1716 (Apr. 1999).

[0007] Inhibitors of $K_v1.5$ and other $K_v1.x$ channels stimulate gastrointestinal motility. Thus, the compounds of the invention are believed to be useful in treating motility disorders such as reflux esophagitis. See Frey et al., "Blocking of cloned and native delayed rectifier K channels from visceral smooth muscles by phencyclidine," *Neurogastroenterol. Motil.*, 12(6):509-516 (Dec. 2000); Hatton et al., "Functional and molecular expression of a voltage-dependent K(+) channel ($K_v1.1$) in interstitial cells of Cajal," *J. Physiol.*, 533(Pt 2):315-327 (Jun. 1, 2001); Vianna-Jorge et al., "Shaker-type K_v1 channel blockers increase the peristaltic activity of guinea-pig ileum by stimulating acetylcholine and tachykinins release by the enteric nervous system," *Br. J. Pharmacol.*, 138(1):57-62 (Jan. 2003); Koh et al., "Contribution of delayed rectifier potassium currents to the electrical activity of murine colonic smooth muscle," *J. Physiol.*, 515(Pt. 2):475-487 (Mar. 1, 1999).

[0008] Inhibitors of $K_v1.5$ relax pulmonary artery smooth muscle. Thus, the compounds of the invention are believed to be useful in treating hypertension and otherwise improving vascular health. See Davies et al., "K_v channel subunit expression in rat pulmonary arteries," *Lung*, 179(3):147-161 (2001), Epub. Feb. 4, 2002; Pozeg et al., "*In vivo* gene transfer of the O2-sensitive potassium channel $K_v1.5$ reduces pulmonary hypertension and restores hypoxic pulmonary vasoconstriction in chronically hypoxic rats," *Circulation*, 107(15):2037-2044 (Apr. 22, 2003), Epub. Apr. 14, 2003.

[0009] Inhibitors of $K_v1.3$ increase insulin sensitivity. Hence, the compounds of the invention are believed to be useful in treating diabetes. See Xu et al., "The voltage-gated potassium channel $K_v1.3$ regulates peripheral insulin sensitivity," *Proc. Natl. Acad. Sci. U.S.A.*, 101(9):3112-3117 (Mar. 2, 2004), Epub. Feb. 23, 2004; MacDonald et al., "Members of the K_v1 and K_v2 voltage-dependent K(+) channel families regulate insulin secretion," *Mol. Endocrinol.*, 15(8):1423-1435 (Aug. 2001); MacDonald et al., "Voltage-dependent K(+) channels in pancreatic beta cells: role,

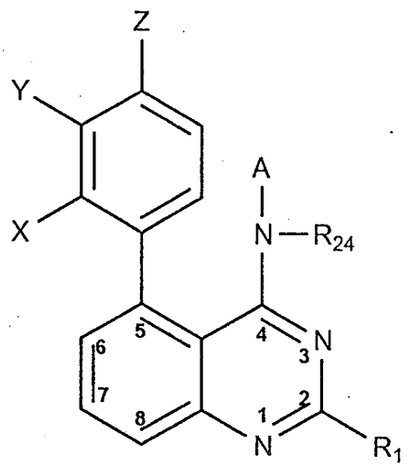
regulation and potential as therapeutic targets," *Diabetologia*, 46(8):1046-1062 (Aug. 2003), Epub. Jun. 27, 2003.

[0010] Stimulation of $K_v1.1$ is believed to reduce seizure activity by hyperpolarizing neurons. Thus, the compounds of the invention are believed to be useful in treating seizures, including seizures associated with epilepsy and other neurological diseases. See Rho et al., "Developmental seizure susceptibility of kv1.1 potassium channel knockout mice," *Dev. Neurosci.*, 21(3-5):320-327 (Nov. 1999); Coleman et al., "Subunit composition of K_v1 channels in human CNS," *J. Neurochem.*, 73(2):849-858 (Aug. 1999); Lopantsev et al., "Hyperexcitability of CA3 pyramidal cells in mice lacking the potassium channel subunit $K_v1.1$," *Epilepsia*, 44(12):1506-1512 (Dec. 2003); Wickenden, "Potassium channels as anti-epileptic drug targets," *Neuropharmacology*, 43(7):1055-1060 (Dec. 2002).

[0011] Inhibition of $K_v1.x$ channels improves cognition in animal models. Thus, the compounds of the invention are believed to be useful in improving cognition and/or treating cognitive disorders. See Cochran et al., "Regionally selective alterations in local cerebral glucose utilization evoked by charybdotoxin, a blocker of central voltage-activated K+-channels," *Eur. J. Neurosci.*, 14(9):1455-1463 (Nov. 2001); Kourrich et al., "Kaliotoxin, a $K_v1.1$ and $K_v1.3$ channel blocker, improves associative learning in rats," *Behav. Brain Res.*, 120(1):35-46 (Apr. 8, 2001).

SUMMARY OF THE INVENTION

[0012] In accordance with the present invention, acyclic compounds and related compounds are provided that have the general structure of formula I:



wherein A, X, Y, Z, R_1 and R_{24} are defined below.

[0013] By use of a respective effective amount of at least one compound described herein, provided are methods of treating (including ameliorating) or preventing arrhythmias, atrial fibrillation, atrial flutter, supraventricular arrhythmias, gastrointestinal disorders (such as reflux esauphagitis or a motility disorder), inflammatory or immunological disease (such as chronic obstructive pulmonary disease), diabetes, cognitive disorders, migraine, epilepsy, hypertension, or treating I_{Kur}-associated conditions, or controlling heart rate.

[0014] Also provided are pharmaceutical compositions comprising a therapeutically effective amount of at least one compound described herein and a pharmaceutically acceptable vehicle or carrier thereof. Such compositions can further comprise one or more other agent(s). For example, at least one other anti-arrhythmic agent (such as sotalol, dofetilide, diltiazem or Verapamil), or at least one calcium channel blocker, or at least one anti-platelet agent (such as clopidogrel, cangrelor, ticlopidine, CS-747, ifetroban and aspirin), or at least one anti-hypertensive agent (such as a beta adrenergic blocker, ACE inhibitor (*e.g.*, captopril, zofenopril, fosinopril, enalapril, ceranopril, cilazopril, delapril, pentopril, quinapril, ramipril, or lisinopril), A II antagonist, ET antagonist, Dual ET/A II antagonist, or vasopepsidase inhibitor (*e.g.*, omapatrilat or gemopatrilat)), or at least one anti thrombotic/anti thrombolytic agent (such as tPA, recombinant tPA, TNK, nPA, factor VIIa inhibitors, factor Xa inhibitors (such as razaxaban), factor XIa inhibitors or thrombin inhibitors),

or at least one anti coagulant (such as warfarin or a heparin), or at least one HMG-CoA reductase inhibitor (pravastatin, lovastatin, atorvastatin, simvastatin, NK-104 or ZD-4522), or at least one anti diabetic agent (such as a biguanide or a biguanide/glyburide combination), or at least one thyroid mimetic, or at least one mineralocorticoid receptor antagonist (such as spironolactone or eplerinone), or at least one cardiac glycoside (such as digitalis or ouabain).

DEFINITIONS

[0015] The terms "alk" or "alkyl" refer to straight or branched chain hydrocarbon groups having 1 to 12 carbon atoms, or 1 to 8 carbon atoms, such as methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, *t*-butyl, pentyl, hexyl, heptyl, octyl, or any subset of the foregoing. The term "substituted alkyl" refers to alkyl groups substituted with one or more groups (such as by groups described above in the definition of R^{10}), such as selected from aryl, substituted aryl, heterocyclo, substituted heterocyclo, carbocyclo, substituted carbocyclo, halo, hydroxy, alkoxy (optionally substituted), aryloxy (optionally substituted), alkylester (optionally substituted), arylester (optionally substituted), alkanoyl (optionally substituted), aryol (optionally substituted), cyano, nitro, amino, substituted amino, amido, lactam, urea, urethane and sulfonyl, or any subset of the foregoing.

[0016] The term "alkenyl" refers to straight or branched chain hydrocarbon groups having 2 to 12 carbon atoms, or 2 to 4 carbon atoms, and at least one double carbon to carbon bond (either cis or trans), such as ethenyl. The term "substituted alkenyl" refers to alkenyl groups substituted with one or more groups (such as by groups described above in the definition of R^{10}), such as selected from aryl, substituted aryl, heterocyclo, substituted heterocyclo, carbocyclo, substituted carbocyclo, halo, hydroxy, alkoxy (optionally substituted), aryloxy (optionally substituted), alkylester (optionally substituted), arylester (optionally substituted), alkanoyl (optionally substituted), aryol (optionally substituted), cyano, nitro, amino, substituted amino, amido, lactam, urea, urethane and sulfonyl, or any subset of the foregoing.

[0017] The term "alkynyl" refers to straight or branched chain hydrocarbon groups having 2 to 12 carbon atoms, or 2 to 4 carbon atoms, and at least one triple

carbon to carbon bond, such as ethynyl. The term "substituted alkynyl" refers to alkynyl groups substituted with one or more groups (such as by groups described above in the definition of R^{10}), such as selected from aryl, substituted aryl, heterocyclo, substituted heterocyclo, carbocyclo, substituted carbocyclo, halo, hydroxy, alkoxy (optionally substituted), aryloxy (optionally substituted), alkylester (optionally substituted), arylester (optionally substituted), alkanoyl (optionally substituted), aryol (optionally substituted), cyano, nitro, amino, substituted amino, amido, lactam, urea, urethane and sulfonyl, or any subset of the foregoing.

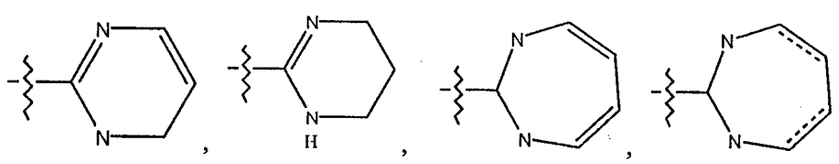
[0018] The term "aryl" refers to aromatic homocyclic (*i.e.*, hydrocarbon) mono-, bi- or tricyclic ring-containing groups such as having 6 to 12 members such as phenyl, naphthyl and biphenyl. Phenyl is an example of an aryl group. The term "substituted aryl" refers to aryl groups substituted with one or more groups (such as by groups described above in the definition of R^{10}), such as selected from alkyl, substituted alkyl, alkenyl (optionally substituted), aryl (optionally substituted), heterocyclo (optionally substituted), halo, hydroxy, alkoxy (optionally substituted), aryloxy (optionally substituted), alkanoyl (optionally substituted), aroyl, (optionally substituted), alkylester (optionally substituted), arylester (optionally substituted), cyano, nitro, amino, substituted amino, amido, lactam, urea, urethane and sulfonyl, or any subset of the foregoing, where optionally one or more pair of substituents together with the atoms to which they are bonded form a 3 to 7 member ring.

[0019] The term "cycloalkyl" refers to mono-, bi- or tri homocyclic ring groups of 3 to 15 carbon atoms which are, respectively, fully saturated and partially unsaturated. The rings of multi-ring cycloalkyl groups may be fused, bridged and/or joined through one or more spiro unions. The term "substituted cycloalkyl" refers to a cycloalkyl group substituted with one or more groups (such as by groups described above in the definition of R^{10}), such as selected from aryl, substituted aryl, heterocyclo, substituted heterocyclo, carbocyclo, substituted carbocyclo, halo, hydroxy, alkoxy (optionally substituted), aryloxy (optionally substituted), alkylester (optionally substituted), arylester (optionally substituted), alkanoyl (optionally substituted), aryol (optionally substituted), cyano, nitro, amino, substituted amino, amido, lactam, urea, urethane and sulfonyl, or any subset of the foregoing.

[0020] The terms "halogen" and "halo" refer to fluorine, chlorine, bromine and iodine.

[0021] The terms "heterocycle", "heterocyclic", "heterocyclic group" or "heterocyclo" refer to fully saturated or partially or completely unsaturated, including aromatic ("heteroaryl") or nonaromatic cyclic groups (for example, 3 to 13 ring member monocyclic, 7 to 17 ring member bicyclic, or 10 to 20 ring member tricyclic ring systems, such as, in certain embodiments, a monocyclic or bicyclic ring containing a total of 3 to 10 ring atoms) which have at least one heteroatom in at least one carbon atom-containing ring. Each ring of the heterocyclic group containing a heteroatom may have 1, 2, 3 or 4 heteroatoms selected from nitrogen atoms, oxygen atoms and/or sulfur atoms, where the nitrogen and sulfur heteroatoms may optionally be oxidized and the nitrogen heteroatoms may optionally be quaternized. The heterocyclic group may be attached at any heteroatom or carbon atom of the ring or ring system. The rings of multi-ring heterocycles may be fused, bridged and/or joined through one or more spiro unions.

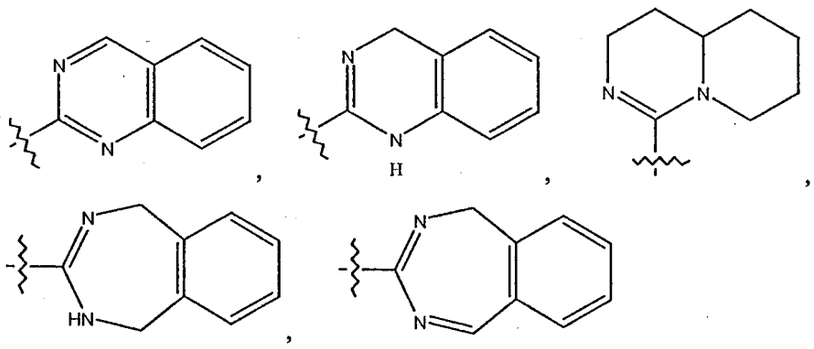
[0022] Exemplary monocyclic heterocyclic groups include azetidinyl, pyrrolidinyl, pyrrolyl, pyrazolyl, oxetanyl, pyrazolinyl, imidazolyl, imidazolinyl, imidazolidinyl, oxazolyl, oxazolidinyl, isoxazolinyl, isoxazolyl, thiazolyl, thiadiazolyl, thiazolidinyl, isothiazolyl, isothiazolidinyl, furyl, tetrahydrofuryl, thienyl, oxadiazolyl, piperidinyl, piperazinyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolodinyl, 2-oxoazepinyl, azepinyl, 4-piperidonyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, tetrahydropyranyl, tetrazoyl, triazolyl, morpholinyl, thiamorpholinyl, thiamorpholinyl sulfoxide, thiamorpholinyl sulfone, 1,3-dioxolane and tetrahydro-1,1-dioxothienyl,



and the like.

[0023] Exemplary bicyclic heterocyclic groups include indolyl, benzothiazolyl, benzoxazolyl, benzothienyl, quinuclidinyl, quinolinyl, tetra-hydroisoquinolinyl, isoquinolinyl, benzimidazolyl, benzopyranyl, indolizinyl, benzofuryl, benzofuranyl,

dihydrobenzofuranyl, chromonyl, coumarinyl, benzodioxolyl, dihydrobenzodioxolyl, benzodioxinyl, cinnolinyl, quinoxalinyl, indazolyl, pyrrolopyridyl, furopyridinyl (such as furo[2,3-c]pyridinyl, furo[3,2-b]pyridinyl] or furo[2,3-b]pyridinyl), dihydroisoindolyl, dihydroquinazolinyl (such as 3,4-dihydro-4-oxo-quinazolinyl), tetrahydroquinolinyl, azabicycloalkyls (such as 6-azabicyclo[3.2.1]octane), azaspiroalkyls (such as 1,4 dioxa-8-azaspiro[4.5]decane), imidazopyridinyl (such as imidazo[1,5-a]pyridin-3-yl), triazolopyridinyl (such as 1,2,4-triazolo[4,3-a]pyridin-3-yl), and hexahydroimidazopyridinyl (such as 1,5,6,7,8,8a-hexahydroimidazo[1,5-a]pyridin-3-yl),



and the like.

[0024] Exemplary tricyclic heterocyclic groups include carbazolyl, benzidolyl, phenanthrolinyl, acridinyl, phenanthridinyl, xanthenyl and the like.

[0025] The terms "substituted heterocycle", "substituted heterocyclic", "substituted heterocyclic group" and "substituted heterocyclo" refer to heterocycle, heterocyclic and heterocyclo groups substituted with one or more groups (such as by groups described above in the definition of R^{10}), such as selected from alkyl, substituted alkyl, alkenyl, oxo, aryl, substituted aryl, heterocyclo, substituted heterocyclo, carbocyclo (optionally substituted), halo, hydroxy, alkoxy (optionally substituted), aryloxy (optionally substituted), alkanoyl (optionally substituted), aroyl (optionally substituted), alkylester (optionally substituted), arylester (optionally substituted), cyano, nitro, amido, amino, substituted amino, lactam, urea, urethane, sulfonyl, , or any subset of the foregoing, where optionally one or more pair of substituents together with the atoms to which they are bonded form a 3 to 7 member ring.

[0026] The term "alkanoyl" refers to alkyl group (which may be optionally substituted as described above) linked to a carbonyl group (*i.e.*, -C(O)-alkyl). Similarly, the term "aroyl" refers to an aryl group (which may be optionally substituted as described above) linked to a carbonyl group (*i.e.*, -C(O)-aryl).

[0027] Throughout the specification, groups and substituents thereof may be chosen to provide stable moieties and compounds.

[0028] The compounds described herein form salts or solvates which are also within the scope of this invention. Reference to a compound described herein is understood to include reference to salts thereof, unless otherwise indicated. The term "salt(s)", as employed herein, denotes acidic and/or basic salts formed with inorganic and/or organic acids and bases. In addition, when a compound described herein contains both a basic moiety and an acidic moiety, zwitterions ("inner salts") may be formed and are included within the term "salt(s)" as used herein. Pharmaceutically acceptable (*i.e.*, non-toxic, physiologically acceptable) salts are preferred, although other salts are also useful, *e.g.*, in isolation or purification steps which may be employed during preparation. Salts of the compounds described herein may be formed, for example, by reacting a compound with an amount of acid or base, such as an equivalent amount, in a medium such as one in which the salt precipitates or in an aqueous medium followed by lyophilization.

[0029] The compounds described herein which contain a basic moiety may form salts with a variety of organic and inorganic acids. Exemplary acid addition salts include acetates (such as those formed with acetic acid or trihaloacetic acid, for example, trifluoroacetic acid), adipates, alginates, ascorbates, aspartates, benzoates, benzenesulfonates, bisulfates, borates, butyrates, citrates, camphorates, camphorsulfonates, cyclopentanepropionates, digluconates, dodecylsulfates, ethanesulfonates, fumarates, glucoheptanoates, glycerophosphates, hemisulfates, heptanoates, hexanoates, hydrochlorides (formed with hydrochloric acid), hydrobromides (formed with hydrogen bromide), hydroiodides, 2-hydroxyethanesulfonates, lactates, maleates (formed with maleic acid), methanesulfonates (formed with methanesulfonic acid), 2-naphthalenesulfonates, nicotinates, nitrates, oxalates, pectinates, persulfates, 3-phenylpropionates, phosphates, picrates, pivalates, propionates, salicylates, succinates, sulfates (such as

those formed with sulfuric acid), sulfonates (such as those mentioned herein), tartrates, thiocyanates, toluenesulfonates such as tosylates, undecanoates, and the like.

[0030] The compounds described herein which contain an acidic moiety may form salts with a variety of organic and inorganic bases. Exemplary basic salts include ammonium salts, alkali metal salts such as sodium, lithium, and potassium salts, alkaline earth metal salts such as calcium and magnesium salts, salts with organic bases (for example, organic amines) such as benzathines, dicyclohexylamines, hydrabamines (formed with N,N-bis(dehydroabietyl)ethylenediamine), N-methyl-D-glucamines, N-methyl-D-glucamides, *t*-butyl amines, and salts with amino acids such as arginine, lysine and the like.

[0031] Basic nitrogen-containing groups may be quaternized with agents such as lower alkyl halides (*e.g.*, methyl, ethyl, propyl, and butyl chlorides, bromides and iodides), dialkyl sulfates (*e.g.*, dimethyl, diethyl, dibutyl, and diamyl sulfates), long chain halides (*e.g.*, decyl, lauryl, myristyl and stearyl chlorides, bromides and iodides), aralkyl halides (*e.g.*, benzyl and phenethyl bromides), and others.

[0032] Any compound that can be converted *in vivo* to provide the bioactive agent (*i.e.*, the compound of formula I) is a prodrug within the scope and spirit of the invention.

[0033] The term "prodrugs" as employed herein includes esters and carbonates formed by reacting one or more hydroxyls of compounds of formula I with alkyl, alkoxy, or aryl substituted acylating agents employing procedures known to those skilled in the art to generate acetates, pivalates, methylcarbonates, benzoates, and the like.

[0034] Various forms of prodrugs are well known in the art and are described in:

a) Wermuth, C.G. et al., *The Practice of Medicinal Chemistry*, Chapter 31, Academic Press (1996);

b) *Design of Prodrugs*, H. Bundgaard, ed., Elsevier (1985);

c) Bundgaard, H., Chapter 5, "Design and Application of Prodrugs," *A Textbook of Drug Design and Development*, pp. 113-191, P. Krosgaard-Larsen et al., eds., Harwood Academic Publishers (1991); and

d) Testa, B. et al., *Hydrolysis in Drug and Prodrug Metabolism*, Wiley-VCH (2003).

[0035] In addition, compounds described herein are, subsequent to their preparation, preferably isolated and purified to obtain a composition containing an amount by weight equal to or greater than 99% of the compound described herein ("substantially pure" compound), which is then used or formulated as described herein. Such "substantially pure" compounds described herein are also contemplated herein as part of the present invention.

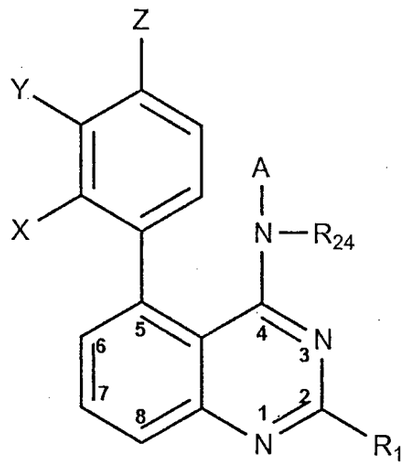
[0036] To the extent that compounds described herein, and salts thereof, may exist in their tautomeric form, all such tautomeric forms are contemplated herein as part of the present invention.

[0037] All stereoisomers of the present compounds, such as those which may exist due to asymmetric carbons on the various substituents, including enantiomeric forms (which may exist even in the absence of asymmetric carbons) and diastereomeric forms are contemplated within the scope of this invention. Individual stereoisomers of the compounds of the invention may, for example, be substantially free of other isomers, or may be admixed, for example, as racemates or with all other, or other selected, stereoisomers.

[0038] The terms "including", "such as", "for example" and the like are intended to refer to exemplary embodiments and not to limit the scope of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

[0039] In accordance with the present invention, compounds of formula I are provided



I

or enantiomers, diastereomers, tautomers, prodrugs or salts thereof wherein:

X is H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CN, -NO_2, -$NR_{11}SO_2R_{12}$, -$SO_2NR_{11}R_{12}$, -$CONR_{11}R_{12}$, -$NR_{11}CONR_{11}R_{12}$, -$NCOR_{11}$, -$NR_{11}SO_2NR_{11}R_{12}$, -$OCONR_{11}R_{12}$, -CO_2R_{11} or -$NR_{11}R_{12}$;

Y is H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CN, -NO_2, -$NR_{11}SO_2R_{12}$, -$SO_2NR_{11}R_{12}$, -$CONR_{11}R_{12}$, -$NR_{11}CONR_{11}R_{12}$, -$NCOR_{11}$, -$NR_{11}SO_2NR_{11}R_{12}$, -$OCONR_{11}R_{12}$, -CO_2R_{11} or -$NR_{11}R_{12}$;

Z is H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CN, -NO_2, -$NR_{11}SO_2R_{12}$, -$SO_2NR_{11}R_{12}$, -$CONR_{11}R_{12}$, -$NR_{11}CONR_{11}R_{12}$, -$NCOR_{11}$, -$NR_{11}SO_2NR_{11}R_{12}$, -$OCONR_{11}R_{12}$, -CO_2R_{11} or -$NR_{11}R_{12}$;

A is -$(CH_2)_m$-R_2, -$CH(R_{25})(R_{26})$, -$(CH_2)_m$-$C(O)$-R_{2a}, –$CH(R_{26})$-CO_2-R_{2a} or –$(CH_2)_{n-1}$-NR_{25}-CO_2-R_{24};

m is 0 to 4;

n is 1 to 4;

n-1 is 2 to 4;

R_1 is -OH, F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{3-10} cycloalkyl, -CN, -$(CH_2)_m$-SO_2R_{11}, -$(CH_2)_n$-$SO_2NR_{11}R_{12}$, -$(CH_2)_n$-CO_2R_{11} or -$(CH_2)_n$-

$NR_{11}SO_2R_{12}$, wherein the alkenyl and cycloalkyl may be optionally substituted with one or more R_{13}'s; or

R_1 is a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein: (i) the heteroaryl and heterocyclyl may be optionally substituted with one or more R_{13a}, R_{13b}, R_{13c}, R_{13d}, R_{13e}, R_{13f}, R_{13g}, R_{13h}, R_{13hh}, R_{13j}, R_{13m}, R_{13m-1}, R_{13n-1}, R_{13p}, R_{13p-1}, R_{13q} and R_{13q-1}; (ii) the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and (iii) the heteroaryl and heterocyclyl are connected to the quinazolinyl ring via a carbon atom; or

R_1 is phenyl, which may be optionally substituted with one or more R_{13aa}, R_{13bb}, R_{13cc}, R_{13dd}, and R_{13ee};

R_2 is C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkenyl or $-NR_{14}R_{14}$, wherein the cycloalkyl may be optionally substituted with one or more R_{13}'s or R_{13bb}'s and the cycloalkenyl may be optionally substituted with one or more R_{13b}'s; provided that R_2 is not $-NR_{14}R_{14}$ when m is 0, 1 or 3; or

R_2 is C_{6-10} aryl, which is optionally substituted with one or more R_{13a-1}, R_{13b-1}, R_{13c-1}, R_{13d-1} and R_{13e-1}; or

R_2 is a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, both of which are optionally substituted with one or more R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d-2}, R_{13e-2}, R_{13g-2}, R_{13a-4}, R_{13b-4}, R_{13c-4}, R_{13d-4}, R_{13b-5}, R_{13c-5}, R_{13h-1}, R_{13hh-1}, R_{13hh-2}, R_{13m-1}, R_{13n-1}, R_{13n-2}, R_{13p-1}, R_{13p-2}, R_{13q-1}, and R_{13q-2}s; and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{2a} is C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, $-NR_{14}R_{14}$, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, any of which is optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{11} and R_{12}, at each occurrence, are independently selected from H, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl and a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{13}'s and the heteroaryl

and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

R_{11} and R_{12} are taken together with the nitrogen to which they are attached to form a 4- to 12-membered heterocyclyl, wherein the heterocyclyl may be optionally substituted with one or more R_{13}'s and the heterocyclyl consists of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; provided that when R_{13} is alkyl substituted with one R_{14a}, R_{14a} is not –OH;

R_{13a}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13aa}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4-

to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13bb}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with

one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl,

alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_n$-$OCONR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{26}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13cc}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$,

$-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$, or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$,

$-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13dd}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, -

$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-

membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13ee}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

$R_{13e\text{-}1}$, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a

4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13f}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13h}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with

one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13h-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl,

alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13j}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13m}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, -

$C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13m-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13n-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$,

$-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, -

$NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl

and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{14}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, $-NO_2$, $-CO_2H$, $-CO_2R_{26}$, $-OCONR_{24}R_{24}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, =O, $-CONR_{24}R_{24}$, $-COR_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$, $-NR_{24}CO_2R_{24}$, $-SO_2NR_{24}R_{24}$, or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{24}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-NO_2$, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, =O, $-CONR_{25}R_{25}$, $-COR_{25}$, $-NR_{25}R_{25}$, $-NR_{25}CO_2R_{25}$, or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1,

2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

[0040] In one embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein R_1 is a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein: (i) the heteroaryl and heterocyclyl may be optionally substituted with one or more R_{13a}, R_{13b}, R_{13c}, R_{13d}, R_{13e}, R_{13f}, R_{13g}, R_{13h}, R_{13hh}, R_{13j}, R_{13m}, R_{13m-1}, R_{13n-1}, R_{13p}, R_{13p-1}, R_{13q} and R_{13q-1}; (ii) the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and (iii) the heteroaryl and heterocyclyl are connected to the quinazolinyl ring via a carbon atom.

[0041] In another embodiments of the invention, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein R_1 is -OH, F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{3-10} cycloalkyl, -CN, $-(CH_2)_m-SO_2R_{11}$, $-(CH_2)_n-SO_2NR_{11}R_{12}$, $-(CH_2)_n-CO_2R_{11}$ or $-(CH_2)_n-NR_{11}SO_2R_{12}$, wherein the alkenyl and cycloalkyl may be optionally substituted with one or more R_{13}'s.

[0042] In yet another embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein R_2 is C_{6-10} aryl, which is optionally substituted with one or more R_{13a-1}, R_{13b-1}, R_{13c-1}, R_{13d-1} and R_{13e-1}.

[0043] In still yet another embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein R_2 is a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, both of which are

optionally substituted with one or more R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d-2}, R_{13e-2}, R_{13g-2}, R_{13a-4}, R_{13b-4}, R_{13c-4}, R_{13d-4}, $R13_{b-5}$, R_{13c-5}, R_{13h-1}, R_{13hh-1}, R_{13hh-2}, R_{13m-1}, R_{13n-1}, R_{13n-2}, $R13_{p-1}$, R_{13p-2}, R_{13q-1}, and R_{13q-2}s; and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

[0044] In one embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein R_2 is a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, both of which are optionally substituted with one or more R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d-2}, R_{13e-2}, R_{13g-2}, R_{13a-4}, R_{13b-4}, R_{13c-4}, R_{13d-4}, $R13_{b-5}$, R_{13c-5}, R_{13h-1}, R_{13hh-1}, R_{13hh-2}, R_{13m-1}, R_{13n-1}, R_{13n-2}, $R13_{p-1}$, R_{13p-2}, R_{13q-1}, and R_{13q-2}s; and the heteroaryl and heterocyclyl consist of carbon atoms and at least one N heteroatom.

[0045] In yet another embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein:

X is H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CN, $-NO_2$, $-NR_{11}SO_2R_{12}$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-NR_{11}SO_2NR_{11}R_{12}$, $-OCONR_{11}R_{12}$, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

Y is H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CN, $-NO_2$, $-NR_{11}SO_2R_{12}$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-NR_{11}SO_2NR_{11}R_{12}$, $-OCONR_{11}R_{12}$, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

Z is H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 6- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CN, $-NO_2$, $-NR_{11}SO_2R_{12}$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-NR_{11}SO_2NR_{11}R_{12}$, $-OCONR_{11}R_{12}$, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

A is $-(CH_2)_m-R_2$, $-CH(R_{25})(R_{26})$, $-(CH_2)_m-C(O)-R_{2a}$, $-CH(R_{26})-CO_2-R_{2a}$ or $-(CH_2)_{n-1}-NR_{25}-CO_2-R_{24}$;

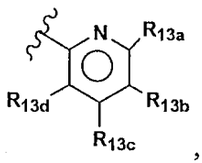
m is 0 to 4;

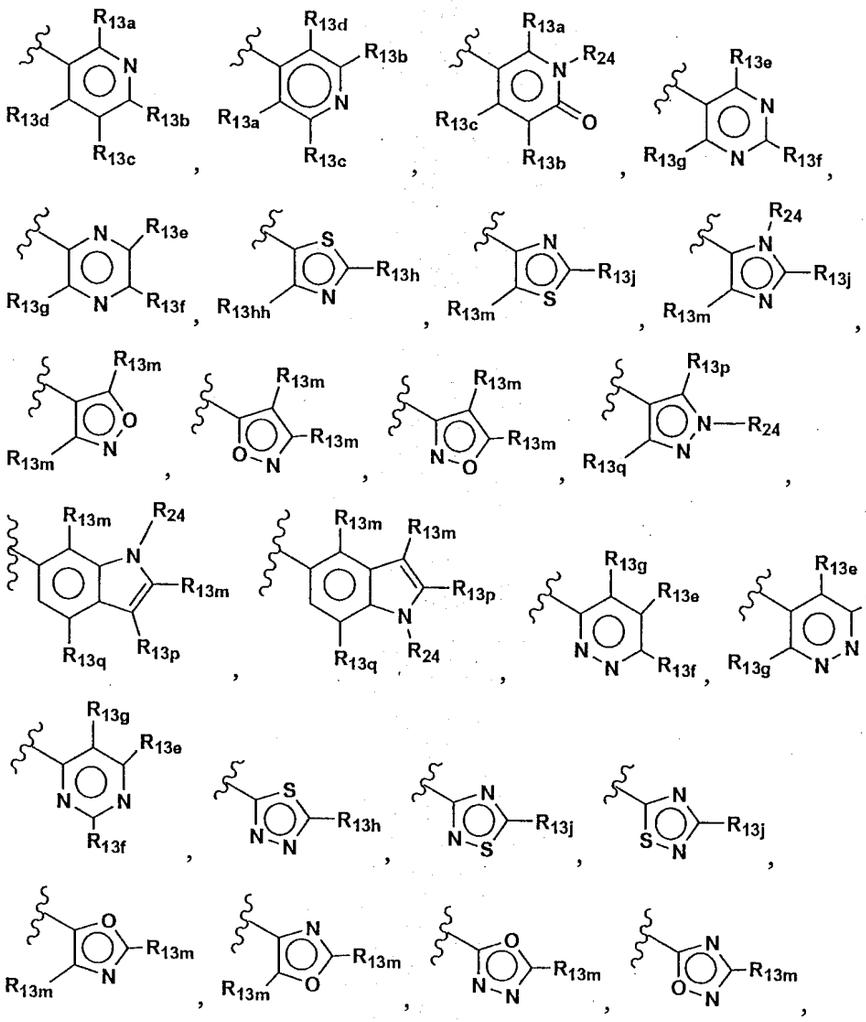
n is 1 to 4;

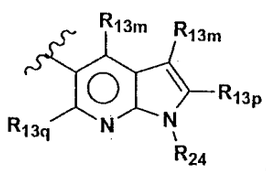
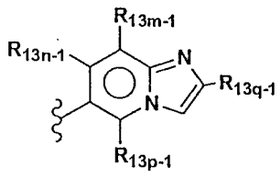
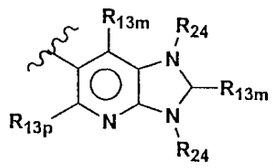
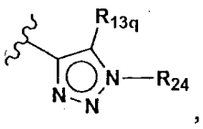
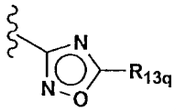
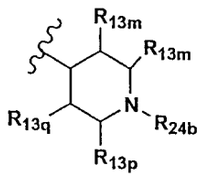
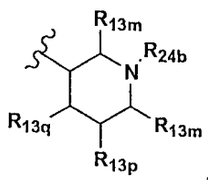
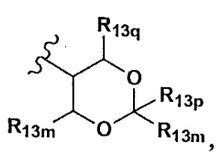
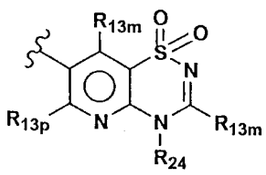
n-1 is 2 to 4;

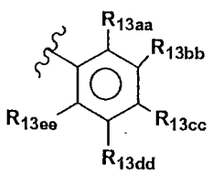
R_1 is -OH, F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{3-10} cycloalkyl, -CN, $-(CH_2)_m-SO_2R_{11}$, $-(CH_2)_n-SO_2NR_{11}R_{12}$, $-(CH_2)_n-CO_2R_{11}$ or $-(CH_2)_n-NR_{11}SO_2R_{12}$, wherein the alkenyl and cycloalkyl may be optionally substituted with one or more R_{13}'s; or

R_1 is selected from the group consisting of:



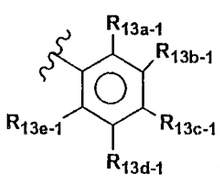











, or ; or



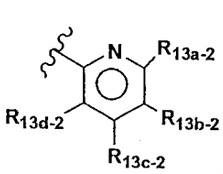
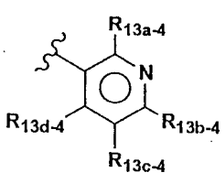
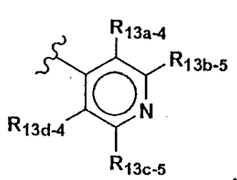
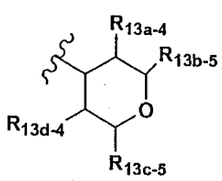
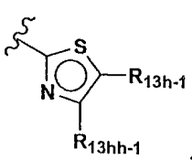
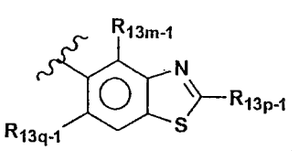
R_1 is ;

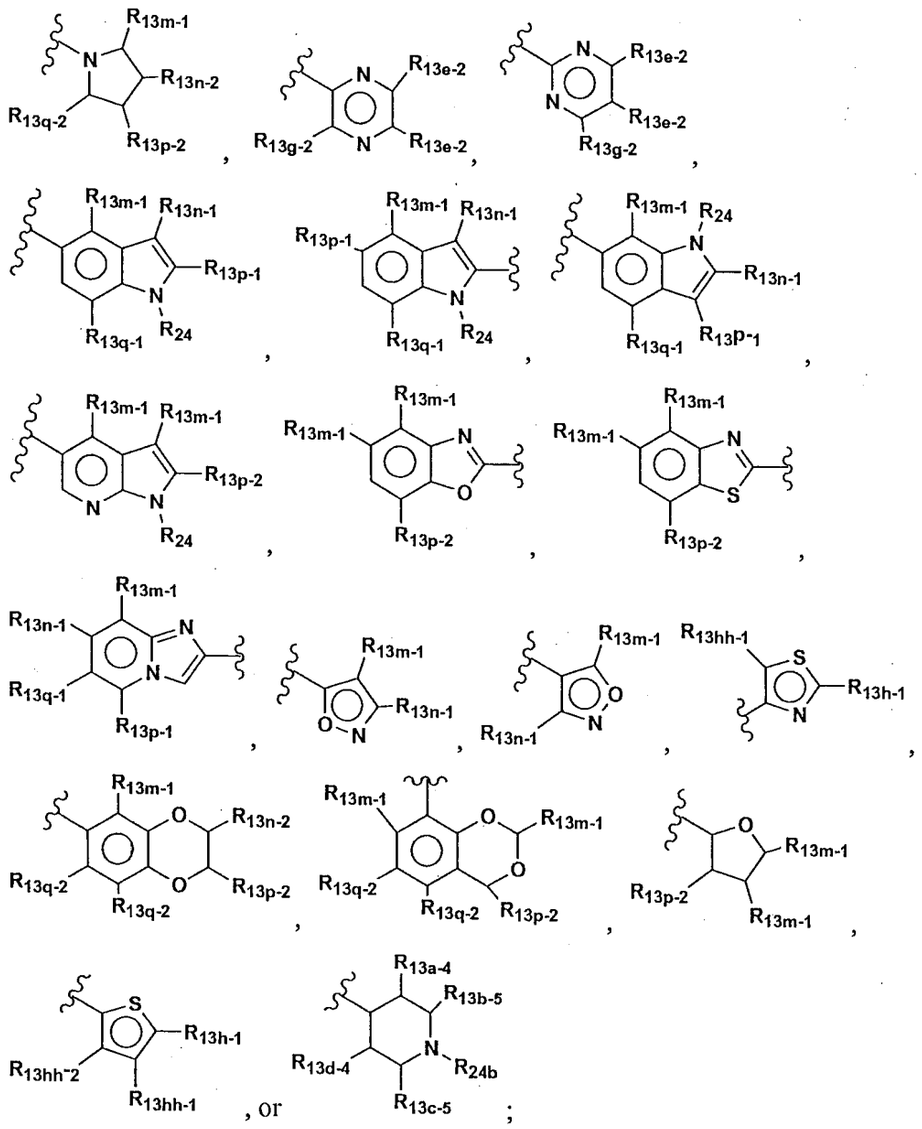
R_2 is $C_{1\text{-}10}$ alkyl, cyclopropyl optionally substituted with one or more R_{13}'s; $C_{4\text{-}10}$ cycloalkyl optionally substituted with one or more R_{13bb}'s; $C_{3\text{-}10}$ cycloalkenyl optionally substituted with one or more R_{13b}'s; or $-NR_{14}R_{14}$; provided that R_2 is not $-NR_{14}R_{14}$ when m is 0, 1 or 3; or



R_2 is ; or

R_2 is selected from the group consisting of:



R_{2a} is C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, $-NR_{14}R_{14}$, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, any of which is optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{11} and R_{12}, at each occurrence, are independently selected from H, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl and a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{13}'s and the heteroaryl

and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

R_{11} and R_{12} are taken together with the nitrogen to which they are attached to form a 4- to 12-membered heterocyclyl, wherein the heterocyclyl may be optionally substituted with one or more R_{13}'s and the heterocyclyl consists of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; provided that when R_{13} is alkyl substituted with one R_{14a}, R_{14a} is not –OH;

R_{13a}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13aa}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4-

to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13bb}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with

one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl,

alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-(CH_2)_n-OCONR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13cc}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$,

$-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$, or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 6- to 12-membered heteroaryl, a 6- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$,

$-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13dd}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, -

$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-

membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13ee}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a

4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13f}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13h}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with

one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13h-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{7-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl,

alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13j}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13m}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -

$C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13m-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13n-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$,

$-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, -

$NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl

and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{14}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, -NO_2, -CO_2H, -CO_2R_{26}, -$OCONR_{24}R_{24}$, -$CO_2NR_{24}R_{24}$, -OCF_3, -OR_{25}, =O, -$CONR_{24}R_{24}$, -COR_{24}, -SO_2R_{24}, -$NR_{24}R_{24}$, -$NR_{24}CO_2R_{24}$, -$SO_2NR_{24}R_{24}$, or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{24}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, -NO_2, -CO_2R_{25}, -OCF_3, -OR_{25}, =O, -$CONR_{25}R_{25}$, -COR_{25}, -$NR_{25}R_{25}$, -$NR_{25}CO_2R_{25}$, or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24b}, at each occurrence, is independently selected from C_{1-10} alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CO_2R_{25}, -$SO_2NR_{25}R_{25}$, -COR_{25} or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and

heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

provide that:

(i) R_1 is not Cl when m is 0, 1 or 2; R_{13a-1} is H, -CF_3, or methoxy; R_{13c-1} is H, OH, methoxy or dimethylamino; X, Y, Z, R_{13b-1}, R_{13d-1}, R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d-2}, R_{13e-2}, R_{13g-2}, R_{13a-4}, R_{13b-4}, R_{13c-4}, R_{13d-4}, R_{13b-5}, R_{13c-5}, R_{13m-1}, R_{13n-1}, R_{13p-1}, and R_{13q-1} are H; and

(ii) m is not 0 or 1 when X, Y, R_{13a}, R_{13d}, R_{13e}, R_{13g}, R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d-2}, R_{13a-4}, R_{13b-4}, R_{13c-4}, R_{13d-4} R_{13b-5}, R_{13c-5}, R_{13h-1} and $R_{13hh-1}$are H; R_{13b} is H or $-SO_2NH_2$; R_{13c} is H, $-CONH_2$, $-SO_2N(C_2H_4OH)_2$, $-SO_2NHCOCH_3$, $-SO_2NH_2$, –tetrazolyl or (4-aminopiperidinyl)sulfonyl; R_{13f} is H or $-NHC_2H_4OCH_3$; and Z is H, -CO_2H, or –CO_2CH_3.

[0046] In still yet another embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein:

X is H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CN, -NO_2, -$NR_{11}SO_2R_{12}$, -$SO_2NR_{11}R_{12}$, -$CONR_{11}R_{12}$, -$NR_{11}CONR_{11}R_{12}$, -$NCOR_{11}$, -$NR_{11}SO_2NR_{11}R_{12}$, -$OCONR_{11}R_{12}$, -CO_2R_{11} or -$NR_{11}R_{12}$;

Y is H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered

heterocyclyl, -CN, -NO_2, -$SO_2NR_{11}R_{12}$, -$CONR_{11}R_{12}$, -$NR_{11}CONR_{11}R_{12}$, -$NCOR_{11}$, -$NR_{11}SO_2NR_{11}R_{12}$, -$OCONR_{11}R_{12}$, -CO_2R_{11} or -$NR_{11}R_{12}$;

Z is H, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 6- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -NO_2, -$NR_{11}SO_2R_{12}$, -$SO_2NR_{11}R_{12}$, -$NR_{11}CONR_{11}R_{12}$, -$NCOR_{11}$, -$NR_{11}SO_2NR_{11}R_{12}$, -$OCONR_{11}R_{12}$, -CO_2R_{11} or -$NR_{11}R_{12}$;

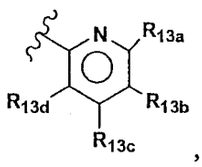
A is -$(CH_2)_m$-R_2, -$CH(R_{25})(R_{26})$, –$CH(R_{26})$-CO_2-R_{2a} or –$(CH_2)_{n-1}$-NR_{25}-CO_2-R_{24};

m is 0 to 4;

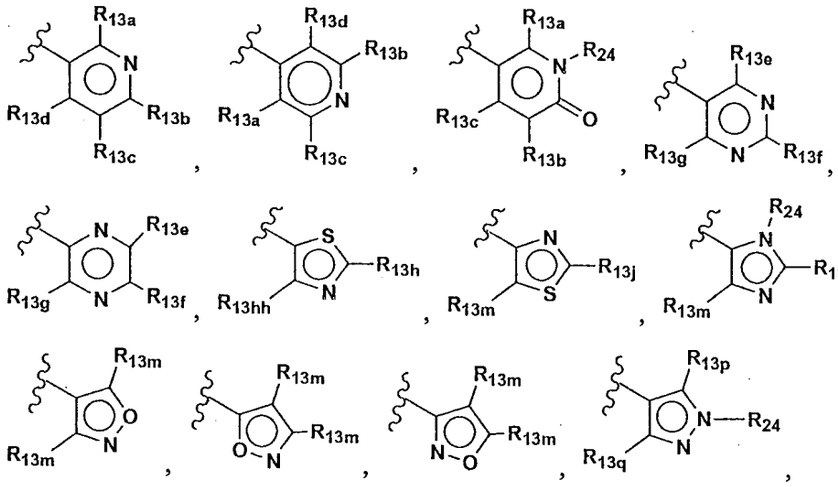
n is 1 to 4;

n-1 is 2 to 4;

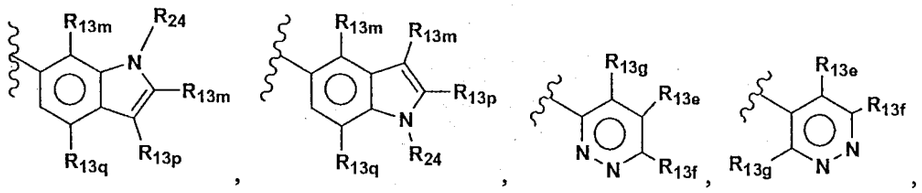
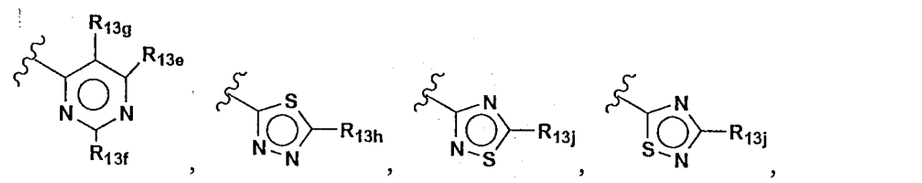
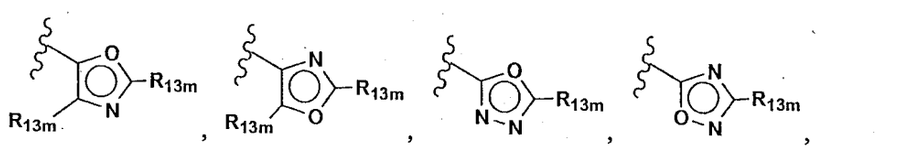
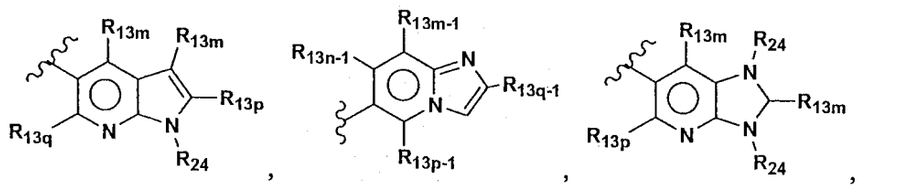
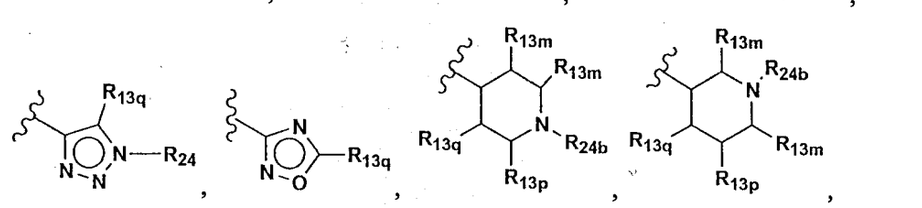
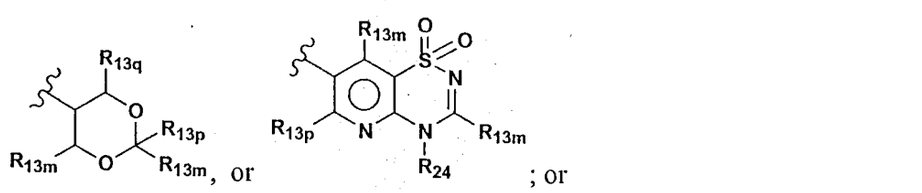
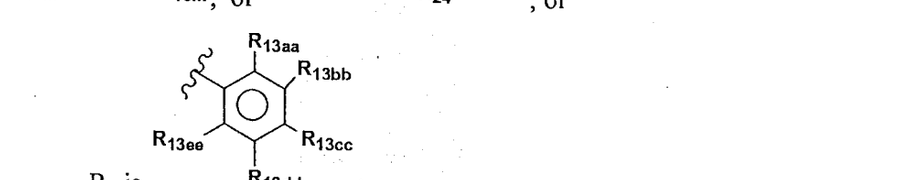
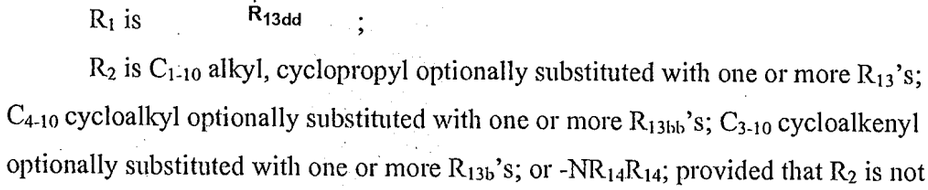
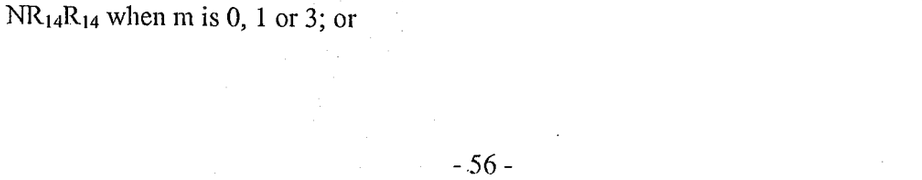
R_1 is -OH, F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{3-10} cycloalkyl, -CN, -$(CH_2)_n$-$SO_2NR_{11}R_{12}$, -$(CH_2)_n$-CO_2R_{11} or -$(CH_2)_n$-$NR_{11}SO_2R_{12}$, wherein the alkenyl and cycloalkyl may be optionally substituted with one or more R_{13}'s; or



R_1 is selected from the group consisting of:



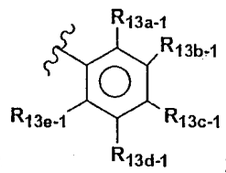
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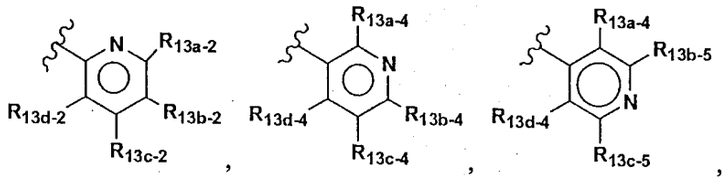
R_1 is ;

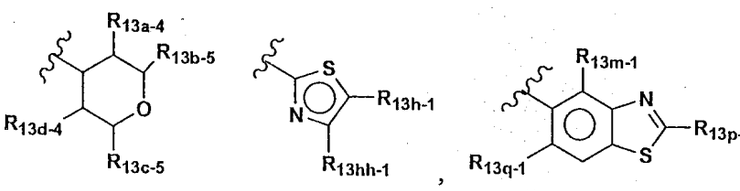
R_2 is $C_{1\text{-}10}$ alkyl, cyclopropyl optionally substituted with one or more R_{13}'s; $C_{4\text{-}10}$ cycloalkyl optionally substituted with one or more R_{13bb}'s; $C_{3\text{-}10}$ cycloalkenyl optionally substituted with one or more R_{13b}'s; or $-NR_{14}R_{14}$; provided that R_2 is not $-NR_{14}R_{14}$ when m is 0, 1 or 3; or

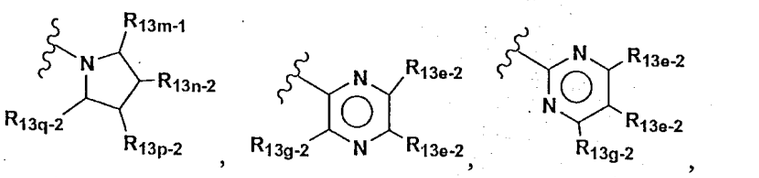


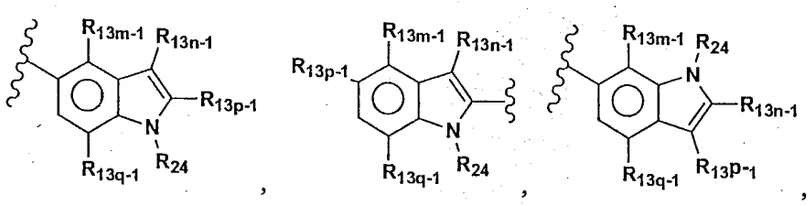
R_2 is ; or

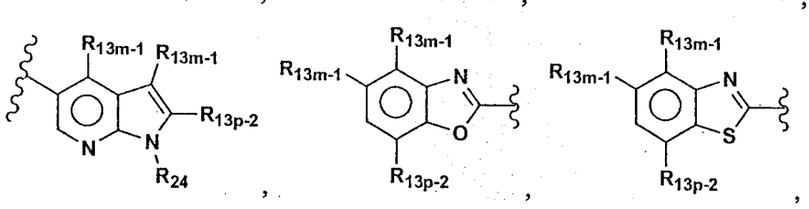
R_2 is selected from the group consisting of:

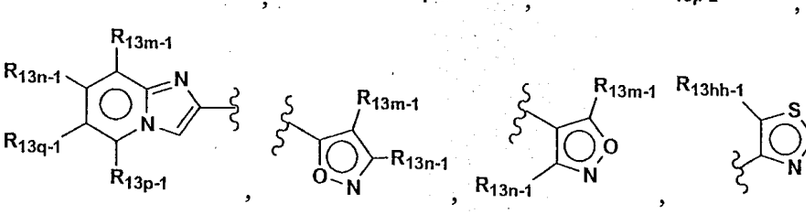


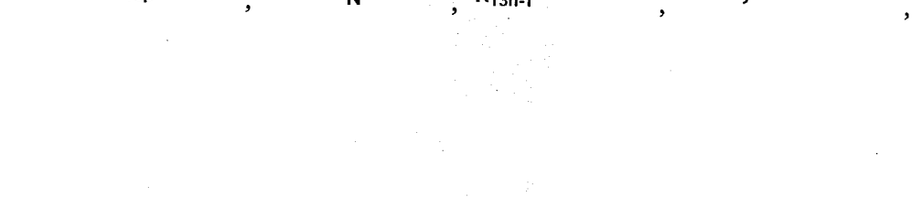


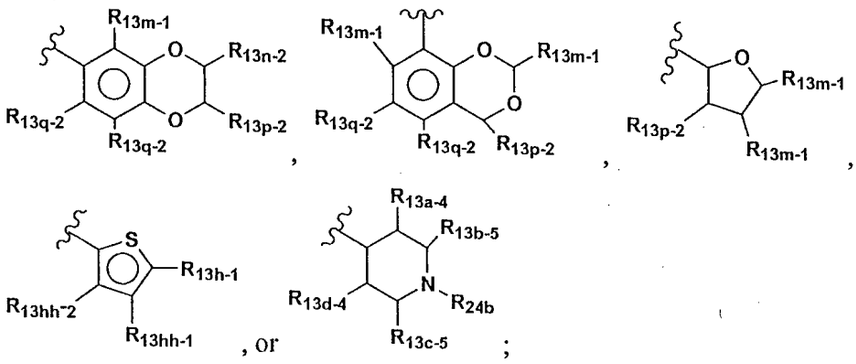












R_{2a} is C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, $-NR_{14}R_{14}$, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, any of which is optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{11} and R_{12}, at each occurrence, are independently selected from H, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl and a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

R_{11} and R_{12} are taken together with the nitrogen to which they are attached to form a 4- to 12-membered heterocyclyl, wherein the heterocyclyl may be optionally substituted with one or more R_{13}'s and the heterocyclyl consists of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl,

alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; provided that when R_{13} is alkyl substituted with one R_{14a}, R_{14a} is not –OH;

R_{13a}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13aa}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

$R_{13a\text{-}1}$, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$,

$-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2}, at each occurrence, is independently H, -OH, F, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, -

$CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13bb}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-$

$SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-NO_2$, $-(CH_2)_m-$

SO_2R_{14}, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-(CH_2)_n-OCONR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13cc}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$, or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 6- to 12-membered heteroaryl, a 6- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, $-NO_2$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-NR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-

membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-4}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4-

to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13dd}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with

one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13ee}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-1}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl,

alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13f}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -

$C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13h}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13h-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{7-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$,

$-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13j}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, -

$CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13m}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13m-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13n-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, -

$CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-

membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a

4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{14}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, -NO_2, -CO_2R_{26}, -$CO_2NR_{24}R_{24}$, -OCF_3, -OR_{25}, =O, -$CONR_{24}R_{24}$, -COR_{24}, -SO_2R_{24}, -$NR_{24}R_{24}$, -$NR_{24}CO_2R_{24}$, -$SO_2NR_{24}R_{24}$, or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{24}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, -NO_2, -CO_2R_{25}, -OCF_3, -OR_{25}, =O, -$CONR_{25}R_{25}$, -COR_{25}, -$NR_{25}R_{25}$, -$NR_{25}CO_2R_{25}$, or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24b}, at each occurrence, is independently selected from C_{1-10} alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CO_2R_{25}, -$SO_2NR_{25}R_{25}$, -COR_{25} or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

provide that:

(i) R_1 is not Cl when m is 0, 1 or 2; R_{13a-1} is H, -CF_3, or methoxy; R_{13c-1} is H, OH, methoxy or dimethylamino; X, Y, Z, R_{13b-1}, R_{13d-1}, R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d-2}, R_{13e-2}, R_{13g-2}, R_{13a-4}, R_{13b-4}, R_{13c-4}, R_{13d-4}, R_{13b-5}, R_{13c-5}, R_{13m-1}, R_{13n-1}, R_{13p-1}, and R_{13q-1} are H; and

(ii) m is not 0 or 1 when X, Y, R_{13a}, R_{13d}, R_{13e}, R_{13g}, R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d-2}, R_{13a-4}, R_{13b-4}, R_{13c-4}, R_{13d-4} R_{13b-5}, R_{13c-5}, R_{13h-1} and $R_{13hh-1}$are H; R_{13b} is H or $-SO_2NH_2$;

R_{13c} is H, $-CONH_2$, $-SO_2N(C_2H_4OH)_2$, $-SO_2NHCOCH_3$, $-SO_2NH_2$, –tetrazolyl or (4-aminopiperidinyl)sulfonyl; R_{13f} is H or $-NHC_2H_4OCH_3$; and Z is H, $-CO_2H$, or $-CO_2CH_3$.

[0047] In one embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein X is H.

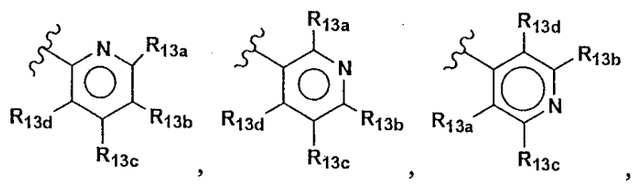
[0048] In another embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein X and Y are H.

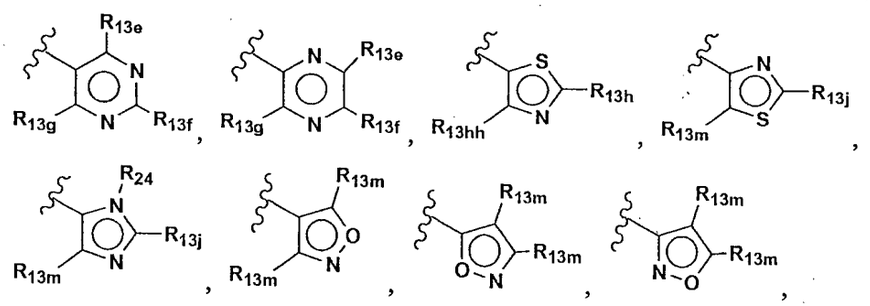
[0049] In yet another embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein X, Y and Z are H.

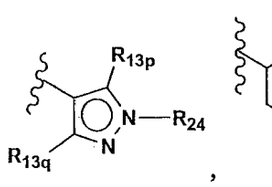
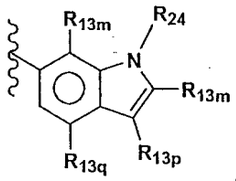
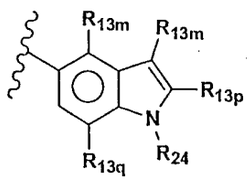
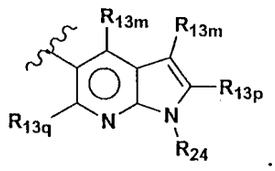
[0050] In one embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein R_1 is F, Cl, Br or I.

[0051] In one embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein R_1 is Cl.

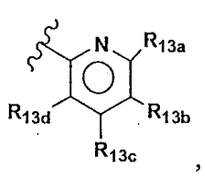
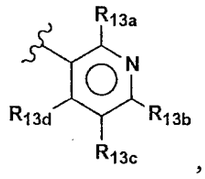
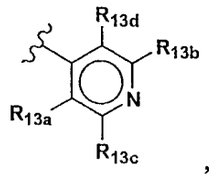
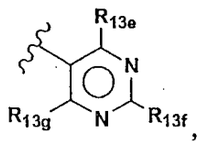
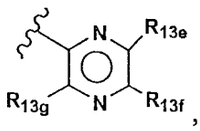
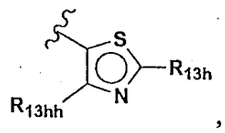
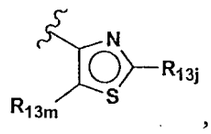
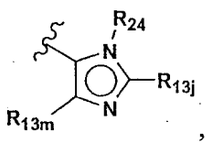
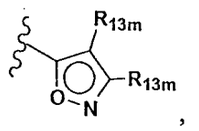
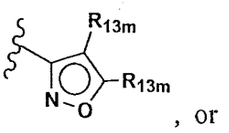
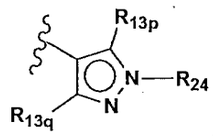
[0052] In one embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein R_1 is selected from the group consisting of:



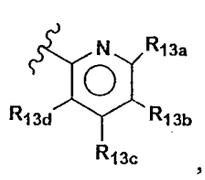
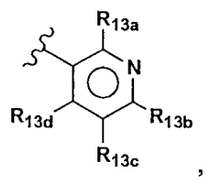


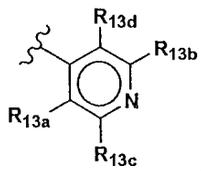
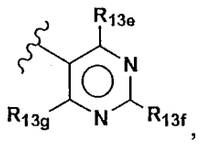
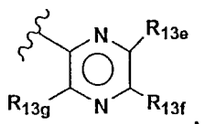
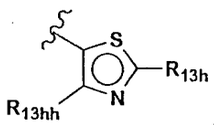
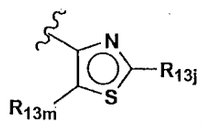
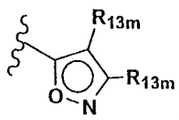
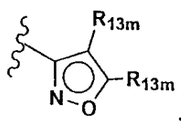



or


[0053] In another embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein R_1 is selected from the group consisting of:

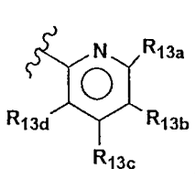
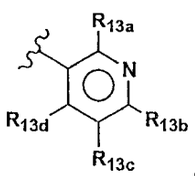
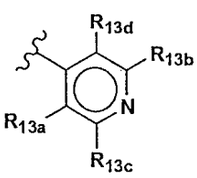
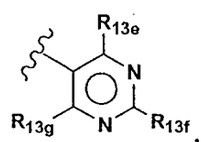
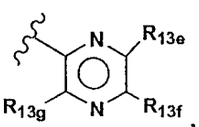
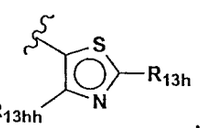
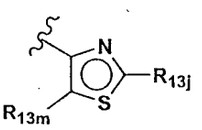
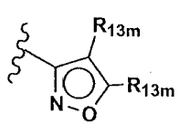










, or


[0054] In yet another embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein R_1 is selected from the group consisting of:

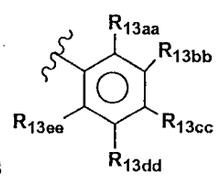



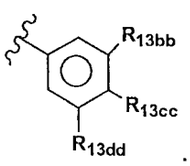
[0055] In one embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein R_1 is selected from the group consisting of:

[0056] In one embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein R_1 is



[0057] In one embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein R_1 is



[0058] In one embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein:

X is H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CN, -NO_2, -$SO_2NR_{11}R_{12}$, -$CONR_{11}R_{12}$, -$NR_{11}CONR_{11}R_{12}$, -$NCOR_{11}$, -CO_2R_{11} or -$NR_{11}R_{12}$;

Y is H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CN, -NO_2, -$SO_2NR_{11}R_{12}$, -$CONR_{11}R_{12}$, -$NR_{11}CONR_{11}R_{12}$, -$NCOR_{11}$, -CO_2R_{11} or -$NR_{11}R_{12}$;

Z is H, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 6- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -NO_2, -$SO_2NR_{11}R_{12}$, -$NCOR_{11}$, -$NR_{11}SO_2NR_{11}R_{12}$, -$OCONR_{11}R_{12}$ or -$NR_{11}R_{12}$;

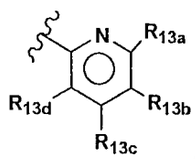
A is -$(CH_2)_m$-R_2, -$CH(R_{25})(R_{26})$ or –$CH(R_{26})$-CO_2-R_{2a};

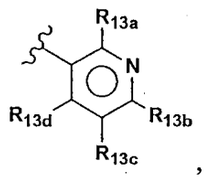
m is 0 to 4;

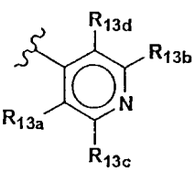
n is 1 to 4;

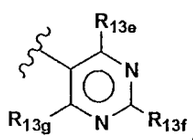
R_1 is -OH, F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{3-10} cycloalkyl, -CN, -$(CH_2)_n$-$SO_2NR_{11}R_{12}$ or -$(CH_2)_n$-$NR_{11}SO_2R_{12}$, wherein the alkenyl and cycloalkyl may be optionally substituted with one or more R_{13}'s; or

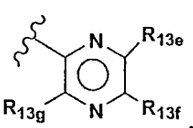
R_1 is selected from the group consisting of:

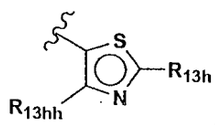


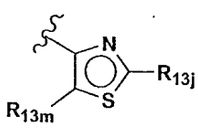


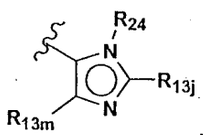


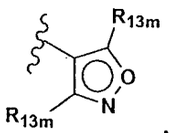


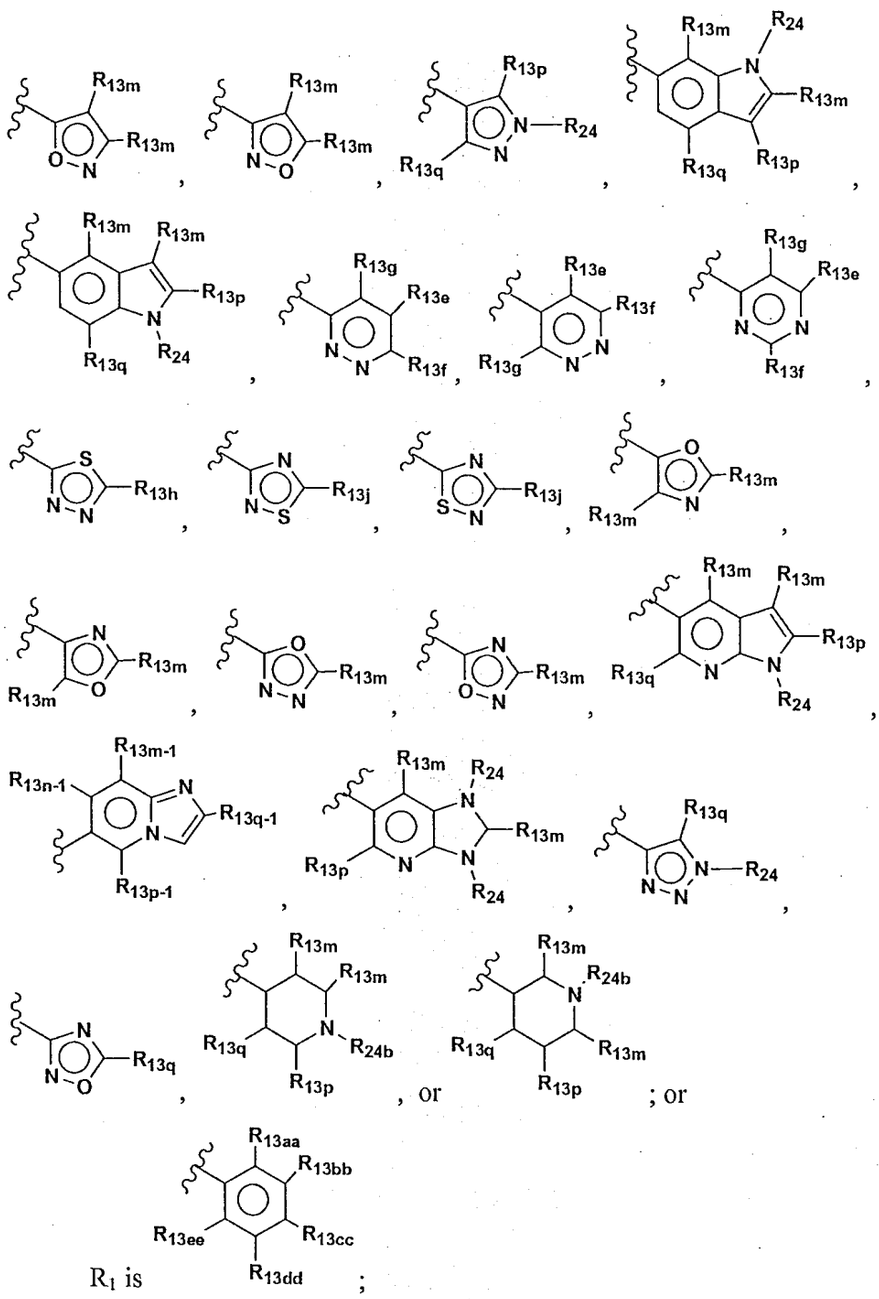






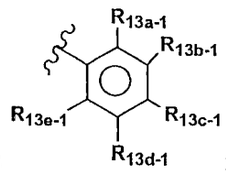






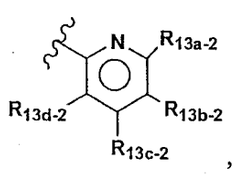
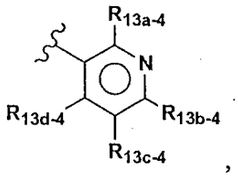
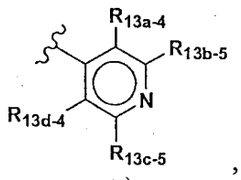
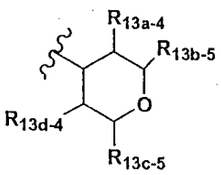
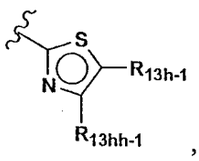
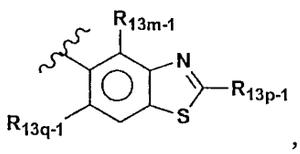
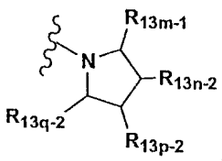
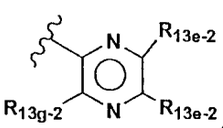
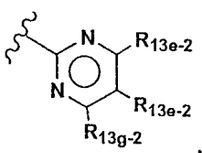
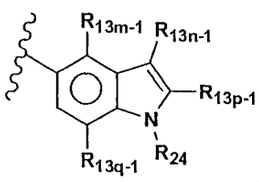
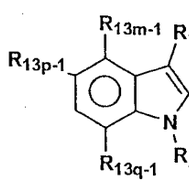
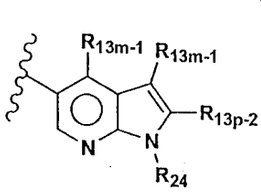
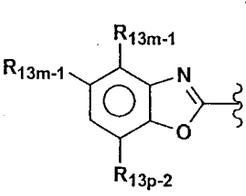
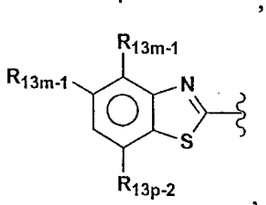
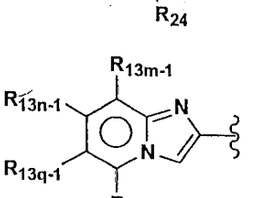
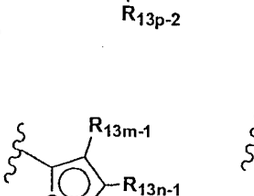
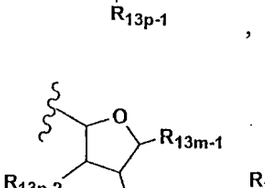
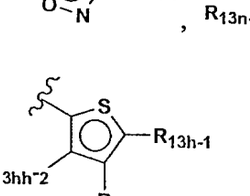
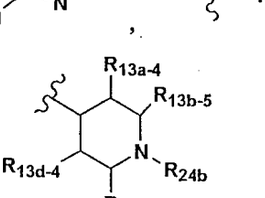
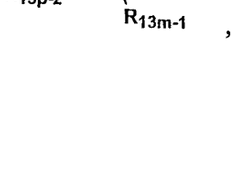
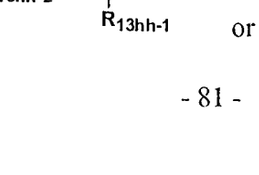
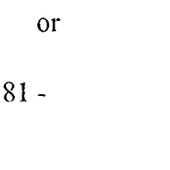
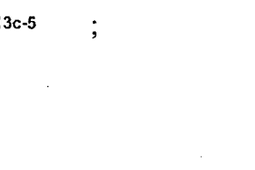
R_1 is ;

R_2 is $C_{1\text{-}10}$ alkyl, cyclopropyl optionally substituted with one or more R_{13}'s; $C_{4\text{-}10}$ cycloalkyl optionally substituted with one or more R_{13bb}'s; or $-NR_{14}R_{14}$; provided that R_2 is not $-NR_{14}R_{14}$ when m is 0, 1 or 3; or



R_2 is ; or

R_2 is selected from the group consisting of:



or ;

R_{2a} is C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, $-NR_{14}R_{14}$, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, any of which is optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{11} and R_{12}, at each occurrence, are independently selected from H, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl and a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

R_{11} and R_{12} are taken together with the nitrogen to which they are attached to form a 4- to 12-membered heterocyclyl, wherein the heterocyclyl may be optionally substituted with one or more R_{13}'s and the heterocyclyl consists of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; provided that when R_{13} is alkyl substituted with one R_{14a}, R_{14a} is not –OH;

R_{13a}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, -

$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13aa}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2}, at each occurrence, is independently H, -OH, F, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered

heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13bb}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to

12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13cc}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 6- to 12-membered heteroaryl, a 6- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, $-NO_2$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-4}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl

and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13dd}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

$R_{13d\text{-}1}$, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

$R_{13d\text{-}2}$, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and

heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13ee}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or –

$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-1}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13f}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, -

$NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13h}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, -

$NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

$R_{13h\text{-}1}$, at each occurrence, is independently H, -OH, F, Cl, Br, I, $C_{1\text{-}10}$ alkyl, $C_{1\text{-}10}$ alkoxy, halo$C_{1\text{-}10}$ alkyl, $C_{3\text{-}10}$ cycloalkyl, $C_{2\text{-}12}$ alkenyl, $C_{2\text{-}12}$ alkynyl, $C_{7\text{-}10}$aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-$C_{1\text{-}10}$ alkyl, -CN, $-NO_2$, $-(CH_2)_m\text{-}SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m\text{-}SO_2NR_{14}R_{14}$, $-(CH_2)_m\text{-}NR_{14}SO_2R_{14}$, $-(CH_2)_n\text{-}NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh}, at each occurrence, is independently H, -OH, F, Cl, Br, I, $C_{1\text{-}10}$ alkyl, $C_{1\text{-}10}$ alkoxy, halo$C_{1\text{-}10}$ alkyl, $C_{3\text{-}10}$ cycloalkyl, $C_{2\text{-}12}$ alkenyl, $C_{2\text{-}12}$ alkynyl, $C_{6\text{-}10}$aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-$C_{1\text{-}10}$ alkyl, -CN, $-NO_2$, $-(CH_2)_m\text{-}SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m\text{-}SO_2NR_{14}R_{14}$, $-(CH_2)_m\text{-}NR_{14}SO_2R_{14}$, $-(CH_2)_n\text{-}NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

$R_{13hh\text{-}1}$, at each occurrence, is independently H, -OH, F, Cl, Br, I, $C_{2\text{-}10}$ alkyl, $C_{1\text{-}10}$ alkoxy, halo$C_{1\text{-}10}$ alkyl, $C_{3\text{-}10}$ cycloalkyl, $C_{2\text{-}12}$ alkenyl, $C_{2\text{-}12}$ alkynyl, $C_{6\text{-}10}$aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-$C_{1\text{-}10}$ alkyl, -CN, $-NO_2$, $-(CH_2)_m\text{-}SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, -

$CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13j}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13m}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered

heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13m-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13n-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4-

to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl

and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{14}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, -NO_2, -CO_2R_{26}, -$OCONR_{24}R_{24}$, -$CO_2NR_{24}R_{24}$, -OCF_3, -OR_{25}, -$CONR_{24}R_{24}$, -COR_{24}, -SO_2R_{24}, -$NR_{24}R_{24}$, -$NR_{24}CO_2R_{24}$, -$SO_2NR_{24}R_{24}$, or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{24}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, -NO_2, -CO_2R_{25}, -OCF_3, -OR_{25}, -$CONR_{25}R_{25}$, -

COR_{25}, $-NR_{25}R_{25}$, $-NR_{25}CO_2R_{25}$, or $C_{6-10}arylC_{1-10}alkyl$, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24b}, at each occurrence, is independently selected from C_{1-10} alkyl, $C_{6-10}aryl$, $C_{3-10}cycloalkyl$, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, $-CO_2R_{25}$, $-SO_2NR_{25}R_{25}$ or $C_{6-10}arylC_{1-10}alkyl$, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, $C_{1-10}alkyl$, $C_{3-10}cycloalkyl$, $C_{6-10}aryl$, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from $C_{1-10}alkyl$, $haloC_{1-10}alkyl$, $C_{3-10}cycloalkyl$, $C_{6-10}aryl$, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

[0059] In one embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein:

X is H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, $haloC_{1-10}$ alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CN, $-NO_2$, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

Y is H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, $haloC_{1-10}$ alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CN, $-NO_2$, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

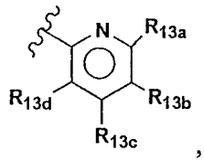
Z is H, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, $haloC_{1-10}$ alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 6- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, $-NO_2$ or $-NR_{11}R_{12}$;

A is $-(CH_2)_m-R_2$ or $-CH(R_{25})(R_{26})$;

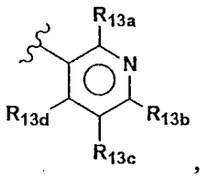
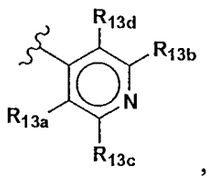
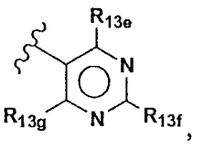
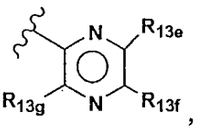
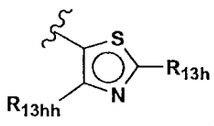
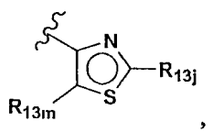
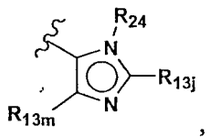
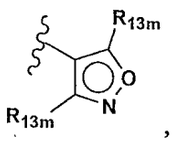
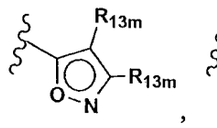
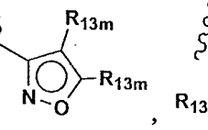
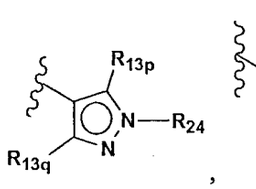
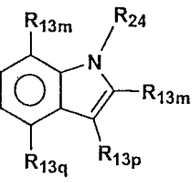
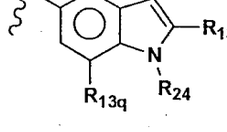
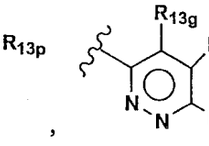
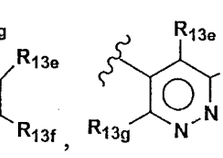
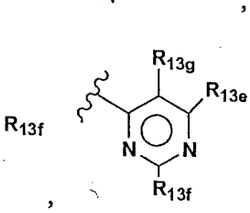
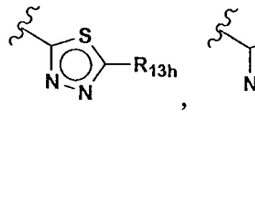
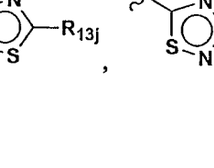
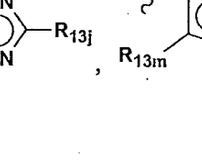
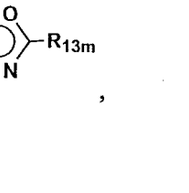
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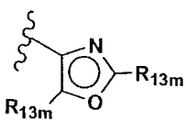
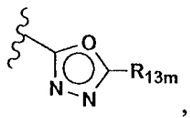
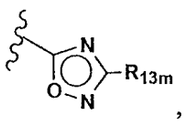
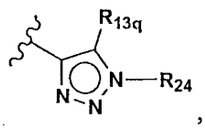
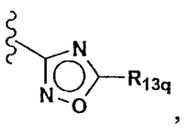
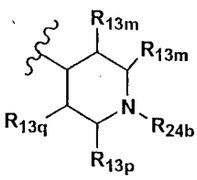
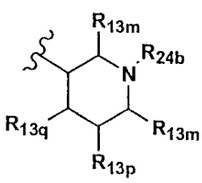
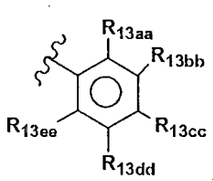
n is 1 to 4;

R_1 is F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{3-10} cycloalkyl, -$(CH_2)_n$-$SO_2NR_{11}R_{12}$ or -$(CH_2)_n$-$NR_{11}SO_2R_{12}$, wherein the alkenyl and cycloalkyl may be optionally substituted with one or more R_{13}'s; or



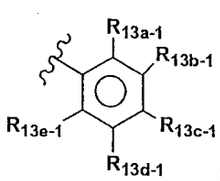
R_1 is selected from the group consisting of:

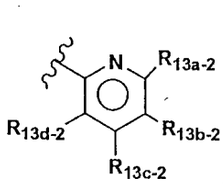
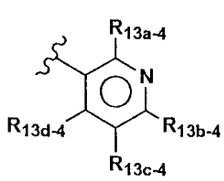
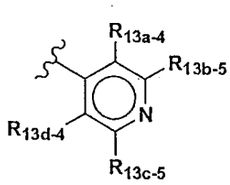
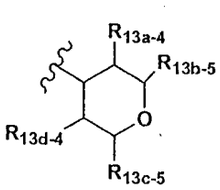
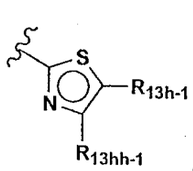
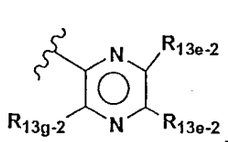
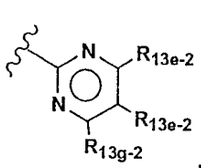
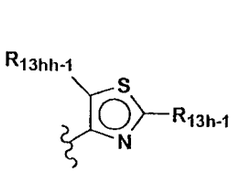
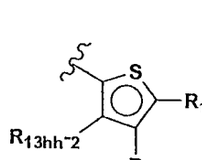
R_1 is ;

R_2 is C_{1-10} alkyl, cyclopropyl optionally substituted with one or more R_{13}'s; or C_{4-10} cycloalkyl optionally substituted with one or more R_{13bb}'s; or



R_2 is ; or

R_2 is selected from the group consisting of:

R_{11} and R_{12}, at each occurrence, are independently selected from H, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl and a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and

heterocyclyl may be optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

R_{11} and R_{12} are taken together with the nitrogen to which they are attached to form a 4- to 12-membered heterocyclyl, wherein the heterocyclyl may be optionally substituted with one or more R_{13}'s and the heterocyclyl consists of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; provided that when R_{13} is alkyl substituted with one R_{14a}, R_{14a} is not –OH;

R_{13a}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13aa}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-1}, at each occurrence, is independently -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2}, at each occurrence, is independently H, -OH, F, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl

and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13bb}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and

heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the

alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13cc}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or –

$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 6- to 12-membered heteroaryl, a 6- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, $-NO_2$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-4}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or –

$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13dd}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$,

$-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$,

$-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13ee}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-1}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-$

$SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13f}, at each occurrence, is independently -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered

heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13h}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13h-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{7-10}aryl, a

4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13j}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13m}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl

and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{14}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more

R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, -NO_2, -CO_2R_{26}, -$CO_2NR_{24}R_{24}$, -OCF_3, -OR_{25}, -$CONR_{24}R_{24}$, -COR_{24}, -SO_2R_{24}, -$NR_{24}R_{24}$, -$NR_{24}CO_2R_{24}$, -$SO_2NR_{24}R_{24}$, or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{24}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, -NO_2, -CO_2R_{25}, -OCF_3, -OR_{25}, -$CONR_{25}R_{25}$, -COR_{25}, -$NR_{25}CO_2R_{25}$, or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24b}, at each occurrence, is independently selected from C_{1-10} alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CO_2R_{25}, -$SO_2NR_{25}R_{25}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered

heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

[0060] In one embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein:

X is H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CO_2R_{11} or -$NR_{11}R_{12}$;

Y is H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CO_2R_{11} or -$NR_{11}R_{12}$;

Z is H, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, a 6- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl or -$NR_{11}R_{12}$;

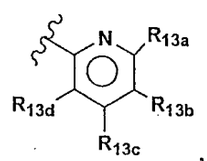
A is -$(CH_2)_m$-R_2 or -$CH(R_{25})(R_{26})$;

m is 0 to 3;

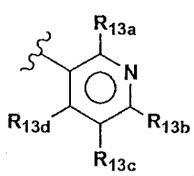
n is 1 to 3;

R_1 is F, Cl, Br, I, C_{1-10} alkyl, C_{2-12} alkenyl, C_{3-10} cycloalkyl, -$(CH_2)_n$-$SO_2NR_{11}R_{12}$ or -$(CH_2)_n$-$NR_{11}SO_2R_{12}$, wherein the alkenyl and cycloalkyl may be optionally substituted with one or more R_{13}'s; or

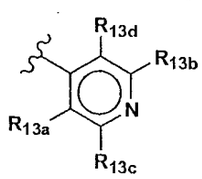
R_1 is selected from the group consisting of:



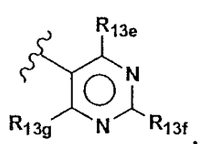
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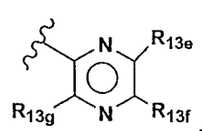
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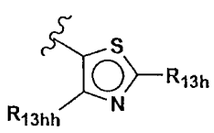
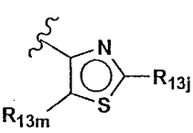
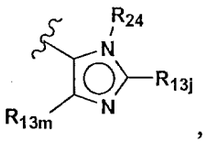
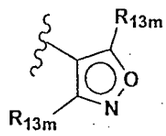
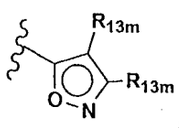
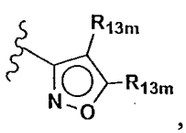
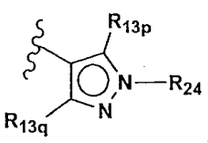
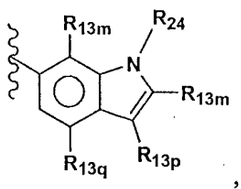
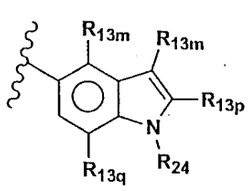
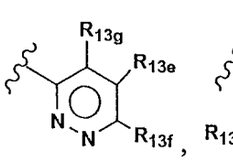
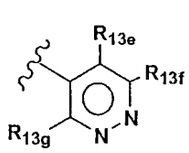
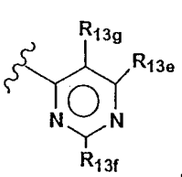
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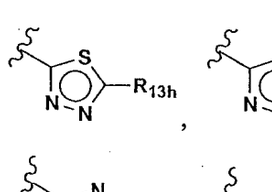
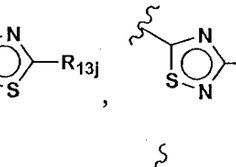
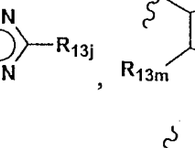
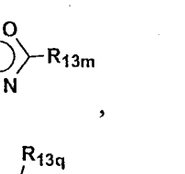
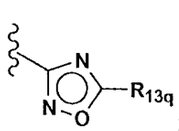
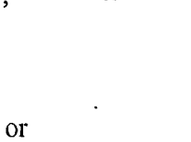


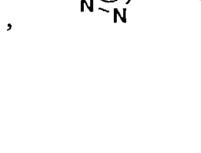
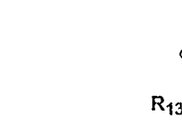
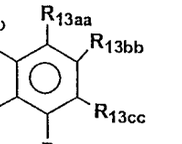
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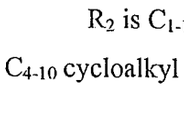
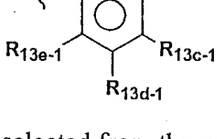


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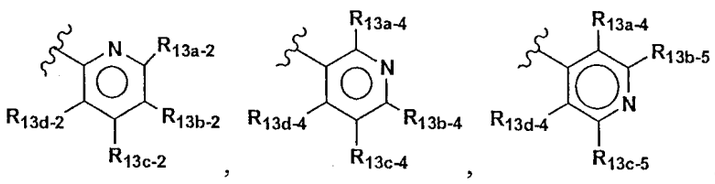



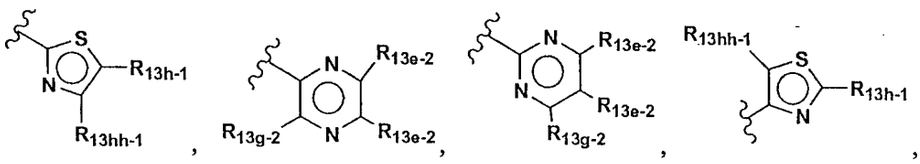
R_1 is ;

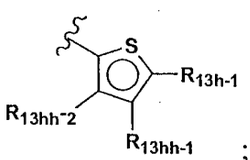
R_2 is $C_{1\text{-}10}$ alkyl, cyclopropyl optionally substituted with one or more R_{13}'s; or $C_{4\text{-}10}$ cycloalkyl optionally substituted with one or more R_{13bb}'s; or

R_2 is ; or

R_2 is selected from the group consisting of:







or ;

R_{11} and R_{12}, at each occurrence, are independently selected from H, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl and a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

R_{11} and R_{12} are taken together with the nitrogen to which they are attached to form a 4- to 12-membered heterocyclyl, wherein the heterocyclyl may be optionally substituted with one or more R_{13}'s and the heterocyclyl consists of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group

consisting of N, S, or O; provided that when R_{13} is alkyl substituted with one R_{14a}, R_{14a} is not –OH;

R_{13a}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13aa}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

$R_{13a\text{-}1}$, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl

and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2}, at each occurrence, is independently H, -OH, F, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally

substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13bb}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl,

cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally

substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13cc}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 6- to 12-membered heteroaryl, a 6- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -NO_2, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of

carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-4}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally

substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13dd}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$ or -CO_2R_{14}, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally

substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13ee}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl,

cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-1}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13f}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy,

aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13h}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl,

cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13h-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{7-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$,

$-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13m}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, -

$NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{14}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, $-NO_2$, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-CONR_{24}R_{24}$, $-COR_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ or C_{6-10}arylC_{1-10}alkyl,

wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{24}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-NO_2$, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-COR_{25}$, $-NR_{25}R_{25}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

[0061] In one embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein:

X is H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, 4- to 12-membered heterocyclyl, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

Y is H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, 4- to 12-membered heterocyclyl, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

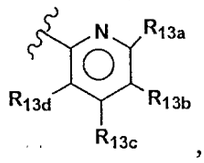
Z is H, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, 4- to 12-membered heterocyclyl or $-NR_{11}R_{12}$;

A is $-(CH_2)_m-R_2$;

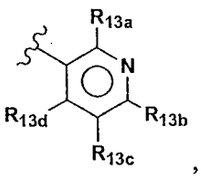
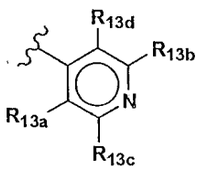
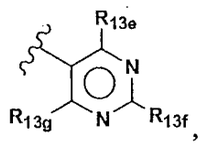
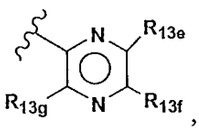
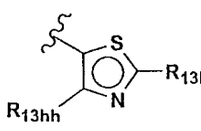
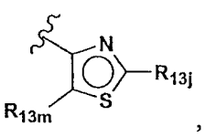
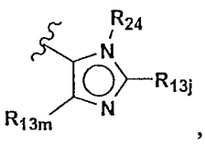
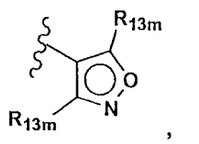
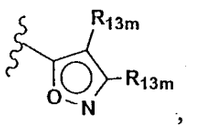
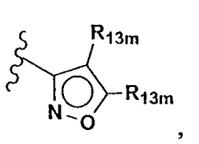
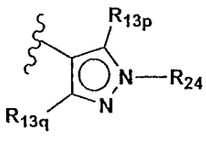
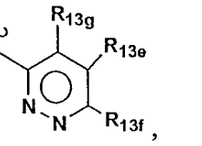
m is 0 to 3;

n is 1 to 3;

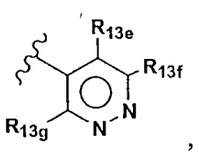
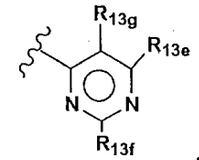
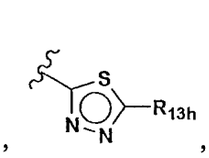
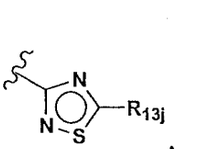
R_1 is F, Cl, Br, I, C_{1-10} alkyl, C_{2-12} alkenyl, C_{3-10} cycloalkyl, wherein the alkenyl and cycloalkyl may be optionally substituted with one or more R_{13}'s; or



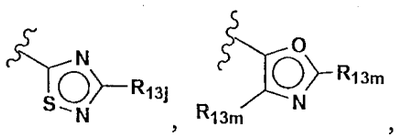
R_1 is selected from the group consisting of:

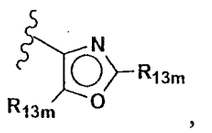
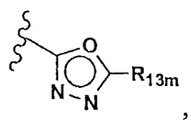
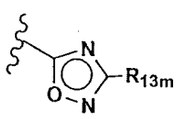
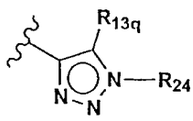
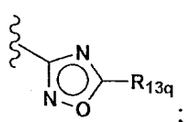
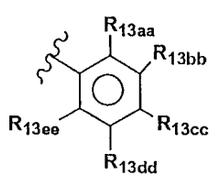













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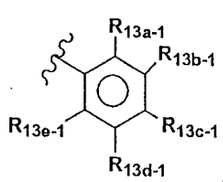




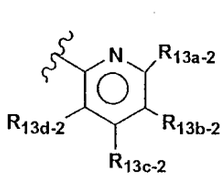
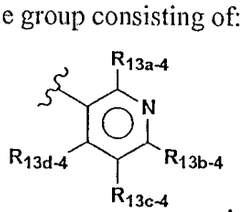
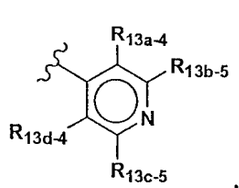
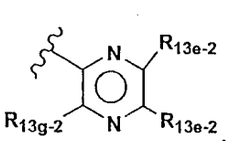
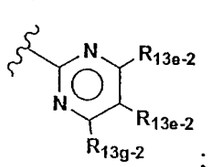
R_1 is ;

R_2 is cyclopropyl optionally substituted with one or more R_{13}'s; or C_{4-10} cycloalkyl optionally substituted with one or more R_{13bb}'s; or



R_2 is ; or

R_2 is selected from the group consisting of:

R_{11} and R_{12}, at each occurrence, are independently selected from H, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl and a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

R_{11} and R_{12} are taken together with the nitrogen to which they are attached to form a 4- to 12-membered heterocyclyl, wherein the heterocyclyl may be optionally

substituted with one or more R_{13}'s and the heterocyclyl consists of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; provided that when R_{13} is alkyl substituted with one R_{14a}, R_{14a} is not –OH;

R_{13a}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13aa}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally

substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2}, at each occurrence, is independently H, -OH, F, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally

substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13bb}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms

and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of

carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -CO_2R_{26} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13cc}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 6- to 12-membered heteroaryl, a 6- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-4}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13dd}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$ or $-CO_2R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13ee}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-1}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13f}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13h}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13m}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of

carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-CONR_{24}R_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

[0062] In yet another embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein:

X is H, F, Cl, Br, I, C_{1-10} alkoxy, haloC_{1-10} alkyl, 4- to 12-membered heterocyclyl, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

Y is H, F, Cl, Br, I, C_{1-10} alkoxy, haloC_{1-10} alkyl, 4- to 12-membered heterocyclyl, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

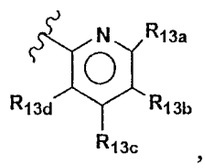
Z is H, Cl, Br, I, C_{1-10} alkoxy, haloC_{1-10} alkyl, 4- to 12-membered heterocyclyl or $-NR_{11}R_{12}$;

A is $-(CH_2)_m-R_2$;

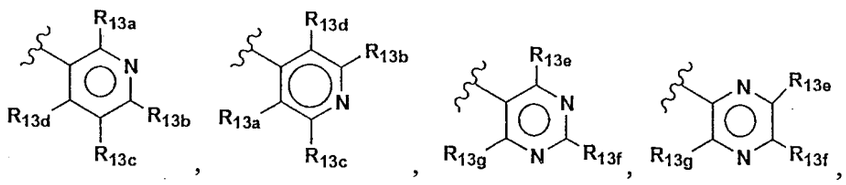
m is 0 to 3;

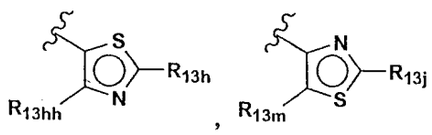
n is 1 to 3;

R_1 is Cl, C_{2-12} alkenyl, C_{3-10} cycloalkyl, wherein the alkenyl and cycloalkyl may be optionally substituted with one or more R_{13}'s; or

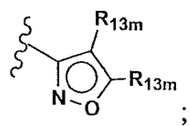


R_1 is selected from the group consisting of:

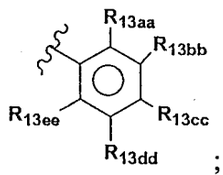




or

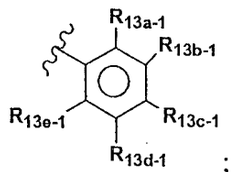


; or



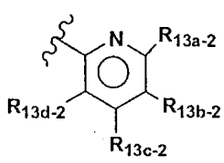
R_1 is ;

R_2 is cyclopropyl optionally substituted with one or more R_{13}'s; or

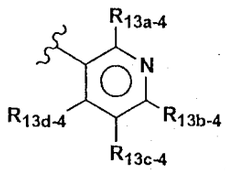


R_2 is ; or

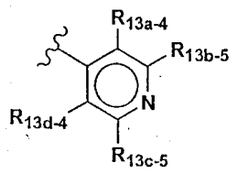
R_2 is selected from the group consisting of:



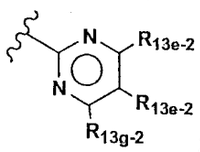
,



,



or



;

R_{11} and R_{12}, at each occurrence, are independently selected from H, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl and a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4

heteroatoms independently selected from the group consisting of N, S, or O; provided that when R_{13} is alkyl substituted with one R_{14a}, R_{14a} is not –OH;

R_{13a}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13aa}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl

and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2}, at each occurrence, is independently H, -OH, F, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more

R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13bb}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more

R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -CO_2R_{26} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the

heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13cc}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 6- to 12-membered heteroaryl, a 6- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-4}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13dd}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$ or -CO_2R_{14}, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13ee}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-1}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13f}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, -CO_2R_{26}, -$CO_2NR_{24}R_{24}$, -OCF_3, -OR_{25}, -$CONR_{24}R_{24}$, -SO_2R_{24}, -$NR_{24}R_{24}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl

and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

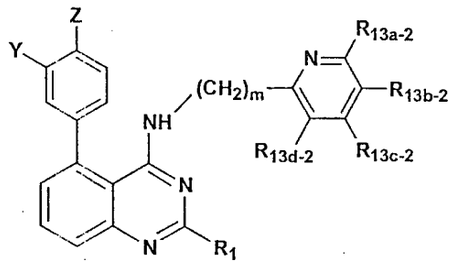
R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

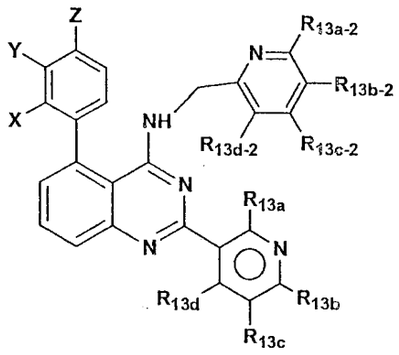
R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

[0063] In yet another embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein the compounds are compounds of formula Ia:



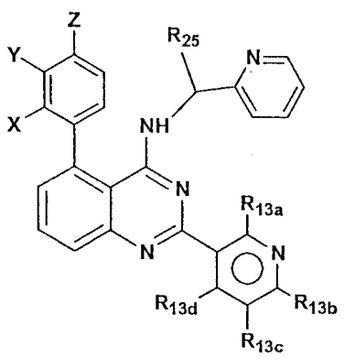
(Ia).

[0064] In yet another embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula I, are provided wherein the compounds are compounds of formula Ib or Ic:



Ib

or



Ic

wherein:

X is H, F, Cl, Br, I, C_{1-10} alkoxy, haloC_{1-10} alkyl, 4- to 12-membered heterocyclyl, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

Y is H, F, Cl, Br, I, C_{1-10} alkoxy, haloC_{1-10} alkyl, 4- to 12-membered heterocyclyl, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

Z is H, Cl, Br, I, C_{1-10} alkoxy, haloC_{1-10} alkyl, 4- to 12-membered heterocyclyl or $-NR_{11}R_{12}$;

R_{11} and R_{12}, at each occurrence, are independently selected from H, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl and a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{13}'s and the heteroaryl

and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2} is independently H, -OH, F, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b} is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$CONR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$ or -$NR_{14}CONR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c} is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, hydroxyC_{1-10} alkyl, cyanoC_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$(CH_2)_n$-$OCONR_{14}R_{14}$, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -CO_2R_{26}, -$NR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$ or -$NR_{14}CONR_{14}R_{14}$, wherein the cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, or 3 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4-

to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2} is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, -CO_2H, -CO_2R_{26}, -$OCONR_{24}R_{24}$, -$CO_2NR_{24}R_{24}$, -OCF_3, -OR_{25}, -$CONR_{24}R_{24}$, -SO_2R_{24}, -$NR_{24}R_{24}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered

heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{24}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

provided that X, Y, Z, R_{13a}, R_{13b}, R_{13d}, R_{13a-2}, R_{13b-2}, R_{13c-2} and R_{13d-2} is not all H when R_{13c} is $-C(=O)N(C_2H_4OCH_3)_2$, $-SO_2N(C_2H_4OH)_2$.

[0065] In yet another embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula Ib are provided.

[0066] In still yet another embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula Ib or Ic, are provided wherein:

X is H, F, Cl, Br, I, C_{1-10} alkoxy, haloC_{1-10} alkyl, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

Y is H, F, Cl, Br, I, C_{1-10} alkoxy, haloC_{1-10} alkyl, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

Z is H, Cl, Br, I, C_{1-10} alkoxy, haloC_{1-10} alkyl or $-NR_{11}R_{12}$;

R_{11} and R_{12}, at each occurrence, are independently selected from H, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl and a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2} is independently H, -OH, F, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b} is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, -

CO_2R_{14}, $-NR_{14}R_{14}$, or $-NR_{14}CONR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c} is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, hydroxyC_{1-10} alkyl, cyanoC_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$, $-NR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$ or $-NR_{14}CONR_{14}R_{14}$, wherein the cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2 or 3 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2} is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of

carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2} is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, -CO_2R_{26}, -$CO_2NR_{24}R_{24}$, -OCF_3, -OR_{25}, -$CONR_{24}R_{24}$, -SO_2R_{24}, -$NR_{24}R_{24}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl

and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

[0067] In one embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula Ib or Ic, are provided wherein:

X is H, F, Cl, Br, I, C_{1-10} alkoxy or haloC_{1-10} alkyl;

Y is H, F, Cl, Br, I, C_{1-10} alkoxy or haloC_{1-10} alkyl;

Z is H, Cl, Br, I, C_{1-10} alkoxy or haloC_{1-10} alkyl;

R_{13a} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4-

to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2} is independently H, -OH, F, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b} is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -CO_2R_{14}, -$NR_{14}R_{14}$, or -$NR_{14}CONR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c} is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, hydroxyC_{1-10} alkyl, cyanoC_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -$NR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$ or -$NR_{14}CONR_{14}R_{14}$, wherein the cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2 or 3 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2} is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more

R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14} is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a} is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24} is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a} is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25} is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26} is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

[0068] In another embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula Ib or Ic, are provided wherein:

X is H, F, Cl, Br, I, or C_{1-10} alkoxy;

Y is H, F, Cl, Br, I, or C_{1-10} alkoxy;

Z is H, Cl, Br, I, C_{1-10} alkoxy or haloC_{1-10} alkyl;

R_{13a} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$CONR_{14}R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2} is independently H, -OH, F, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -$CONR_{14}R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b} is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -CO_2R_{14}, -$NR_{14}R_{14}$, or -$NR_{14}CONR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl

and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c} is independently H, Cl, Br, I, C_{1-10} alkyl, hydroxyC_{1-10} alkyl, cyanoC_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -$NR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$ or -$NR_{14}CONR_{14}R_{14}$, wherein the cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, or 3 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$CONR_{14}R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2} is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$CONR_{14}R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more

R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14} is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a} is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

[0069] In still yet another embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula Ib or Ic, are provided wherein:

X is H, F, Cl, Br, I or C_{1-10} alkoxy;

Y is H, F, Cl, Br, I or C_{1-10} alkoxy;

Z is H, Cl, Br, I or C_{1-10} alkoxy;

R_{13a} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl or -CN, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2} is independently H, -OH, F, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl or a 4- to 12-membered heteroaryl-C_{1-10} alkyl, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b} is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$NR_{14}R_{14}$, or -$NR_{14}CONR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of

carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl or a 4- to 12-membered heteroaryl-C_{1-10} alkyl, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c} is independently H, Cl, Br, I, C_{1-10} alkyl, hydroxyC_{1-10} alkyl, cyanoC_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -$NR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$ or -$NR_{14}CONR_{14}R_{14}$, wherein the cycloalkyl, alkenyl, alkoxy, aryl and heteroaryl may be optionally substituted with one or more R_{14a}'s and the heteroaryl consists of carbon atoms and 1, 2 or 3 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2} is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl or -CN wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

[0070] In one embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula Ib or Ic, are provided wherein:

X is H or C_{1-10} alkoxy;

Y is H or C_{1-10} alkoxy;

Z is H or C_{1-10} alkoxy;

R_{13a}, at each occurrence, is independently H or -CN;

R_{13a-2}, at each occurrence, is independently H, F, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl or C_{3-10} cycloalkyl, wherein the alkyl, cycloalkyl and alkoxy may be optionally substituted with one or more R_{14a}'s;

R_{13b}, at each occurrence, is independently H, C_{1-10} alkoxy, -CN, $-CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}R_{14}$, or $-NR_{14}CONR_{14}R_{14}$;

R_{13b-2}, at each occurrence, is independently H or F;

R_{13c}, at each occurrence, is independently H, C_{1-10} alkyl, C_{1-10} alkoxy, C_{3-10} cycloalkyl, C_{2-12} alkenyl, a 4- to 12-membered heteroaryl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-NR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$ or $-NR_{14}CONR_{14}R_{14}$, wherein the cycloalkyl, alkenyl, alkoxy and heteroaryl may be optionally substituted with one or more R_{14a}'s and the heteroaryl consists of carbon atoms and 1, 2 or 3 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2}, R_{13d}, and R_{13d-2} are H;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon

atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

[0071] In another embodiment, compounds, enantiomers, diastereomers, tautomers, prodrugs or salts thereof, of formula Ib or Ic, are provided wherein:

X, Y, Z, R_{13a}, R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d} and R_{13d-2} are H;

R_{13b}, at each occurrence, is independently H, C_{1-10} alkoxy, or $-NR_{14}R_{14}$;

R_{13c}, at each occurrence, is independently H, C_{1-10} alkyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-CONR_{14}R_{14}$ or $-NR_{14}R_{14}$, wherein the cycloalkyl, and heteroaryl may be optionally substituted with one or more R_{14a}'s and the heteroaryl consists of carbon atoms and 1, 2 or 3 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4-

to 12-membered heterocyclyl, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ or $C_{6-10}arylC_{1-10}alkyl$, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, $C_{1-10}alkyl$, $C_{3-10}cycloalkyl$, $C_{6-10}aryl$, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from $C_{1-10}alkyl$, $haloC_{1-10}alkyl$, $C_{3-10}cycloalkyl$, $C_{6-10}aryl$, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

[0072] In another embodiment, compounds, enantiomers, diastereomers, tautomers, or salt thereof, of the present invention are selected from the compounds exemplified in the examples, preferably, Examples 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 and 137 more preferably, Examples 7, 32, and 101, even more preferably, Examples 7 and 101.

[0073] In one embodiment, pharmaceutical compositions comprising a therapeutically effective amount of at least one compound of formula I, Ia, Ib, and/or Ic, preferably compounds exemplified in the examples, more preferably, Examples 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 and 137, even more preferably, Examples 7, 32, and 101, still even more preferably, Examples 7 and 101, are provided.

[0074] In another embodiment, pharmaceutical compositions comprising a therapeutically effective amount of at least one compound of formula I, Ia, Ib, and/or Ic, preferably compounds exemplified in the examples, more preferably, Examples 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 and 137, even more preferably, Examples 7, 32, and 101, still even more preferably, Examples 7 and 101, and at least one other therapeutic agent, for example, anti-arrhythmic agents,

calcium channel blockers, anti-platelet agents, anti-hypertensive agents, anti thrombotic/anti thrombolytic agents, anti coagulants, HMG-CoA reductase inhibitors, anti diabetic agents, thyroid mimetics, mineralocorticoid receptor antagonists, and cardiac glycosides, are provided.

[0075] In yet another embodiment, pharmaceutical compositions comprising a therapeutically effective amount of at least one compound of formula I, Ia, Ib, and/or Ic, preferably compounds exemplified in the examples, more preferably, Examples 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 and 137, even more preferably, Examples 7, 32, and 101, still even more preferably, Examples 7 and 101, and at least one other therapeutic agent, for example, sotalol, dofetilide, diltiazem, verapamil, clopidogrel, cangrelor, ticlopidine, CS-747, ifetroban, aspirin, a beta adrenergic blocker, an ACE inhibitor, an A II antagonist, an ET antagonist, a dual ET/A II antagonist, a vasopepsidase inhibitor, tPA, recombinant tPA, TNK, nPA, a factor VIIa inhibitor, a factor Xa inhibitor, a factor XIa inhibitor, a thrombin inhibitor, warfarin, a heparin, pravastatin, lovastatin, atorvastatin, simvastatin, NK-104, ZD-4522, a biguanide, a biguanide/glyburide combination, spironolactone, eplerinone, digitalis and ouabain, are provided.

[0076] In still yet another embodiment, pharmaceutical compositions comprising a therapeutically effective amount of at least one compound of formula I, Ia, Ib, and/or Ic, preferably compounds exemplified in the examples, more preferably, Examples 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 and 137, even more preferably, Examples 7, 32, and 101, still even more preferably, Examples 7 and 101, and at least one other therapeutic agent, for example, captopril, zofenopril, fosinopril, enalapril, ceranopril, cilazopril, delapril, pentopril, quinapril, ramipril, lisinopril, omapatrilat, gemopatrilat, and razaxaban, are provided.

[0077] In one embodiment, methods of treating or preventing arrhythmia comprising administering to a patient in need thereof an effective amount of at least one compound of formula I, Ia, Ib, and/or Ic, preferably compounds exemplified in the examples, more preferably, Examples 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 and 137, even more preferably, Examples 7, 32, and 101, still even more preferably, Examples 7 and 101, are provided.

[0078] In another embodiment, methods of treating or preventing supraventricular arrhythmia, for example, atrial fibrillation and atrial flutter, comprising administering to a patient in need thereof an effective amount of at least one compound of formula I, Ia, Ib, and/or Ic, preferably compounds exemplified in the examples, more preferably, Examples 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 and 137, even more preferably, Examples 7, 32, and 101, still even more preferably, Examples 7 and 101, are provided.

[0079] In one embodiment, a method of controlling heart rate comprising administering to a patient in need thereof an effective amount of at least one compound of formula I, Ia, Ib, and/or Ic, preferably compounds exemplified in the examples, more preferably, Examples 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 and 137, even more preferably, Examples 7, 32, and 101, still even more preferably, Examples 7 and 101, is provided.

[0080] In another embodiment, methods of treating an I_{Kur}-associated conditions, for example, gastrointestinal disorders, such as reflux esauphagitis and a motility disorder; inflammatory and/or immunological diseases, such as chronic obstructive pulmonary disease; diabetes; cognitive disorders; migraines; epilepsy; and hypertension, comprising administering to a patient in need thereof an effective amount of at least one compound of formula I, Ia, Ib, and/or Ic, preferably compounds exemplified in the examples, more preferably, Examples 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 and 137, even more preferably, Examples 7, 32, and 101, still even more preferably, Examples 7 and 101, are provided.

[0081] The invention may be embodied in other specific forms without departing from the spirit or essential attributes thereof. This invention also encompasses all combinations of alternative aspects of the invention noted herein. It is understood that any and all embodiments of the present invention may be taken in conjunction with any other embodiment to describe additional embodiments of the present invention. Furthermore, any elements of an embodiment may be combined with any and all other elements from any of the embodiments to describe additional embodiments.

SYNTHESIS

[0082] The compounds of the present invention can be prepared in a number of ways known to one skilled in the art of organic synthesis. The compounds of the present invention can be synthesized using the methods described below, together with synthetic methods known in the art of synthetic organic chemistry, or by variations thereon as appreciated by those skilled in the art. Preferred methods include, but are not limited to, those described below. The reactions are performed in a solvent or solvent mixture appropriate to the reagents and materials employed and suitable for the transformations being effected. It will be understood by those skilled in the art of organic synthesis that the functionality present on the molecule should be consistent with the transformations proposed. This will sometimes require a judgment to modify the order of the synthetic steps or to select one particular process scheme over another in order to obtain a desired compound of the invention.

[0083] The novel compounds of this invention may be prepared using the reactions and techniques described in this section. Also, in the description of the synthetic methods described below, it is to be understood that all proposed reaction conditions, including choice of solvent, reaction atmosphere, reaction temperature, duration of the experiment and workup procedures, are chosen to be the conditions standard for that reaction, which should be readily recognized by one skilled in the art. Restrictions to the substituents that are compatible with the reaction conditions will be readily apparent to one skilled in the art and alternate methods must then be used.

[0084] The compounds of the present invention may be prepared by the exemplary processes described in the following schemes and working examples, as well as relevant published literature procedures that are used by one skilled in the art. Exemplary reagents and procedures for these reactions appear hereinafter and in the working examples. Protection and de-protection of functional groups in the processes below may be carried out by procedures generally known in the art (see, for example, Greene, T.W. et al., *Protecting Groups in Organic Synthesis*, 3rd Ed., Wiley (1999). General methods of organic synthesis and functional group transformations are found in: Trost, B.M. et al., eds., *Comprehensive Organic Synthesis: Selectivity, Strategy & Efficiency in Modern Organic Chemistry*, Pergamon Press, New York, NY (1991);

March, J., *Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, 4th Ed., Wiley & Sons, New York, NY (1992); Katritzky, A.R. et al., eds., *Comprehensive Organic Functional Groups Transformations*, 1st Ed., Elsevier Science Inc., Tarrytown, NY (1995); Larock, R.C., *Comprehensive Organic Transformations*, VCH Publishers, Inc., New York, NY (1989); and references therein.

[0085] Solvents, temperatures, pressures, and other reaction conditions may readily be selected by one of ordinary skill in the art. Starting materials are commercially available or can be readily prepared by one of ordinary skill in the art using known methods. For all of the schemes and compounds described below Y, Z, A, R_1 and R_{24} are as described for a compound of Formula (I).

[0086] The following are the definitions of symbols used throughout Schemes 1 to 3 and the examples:

Me = Methyl

Et = Ethyl

Pr = Propyl

i-Pr = Isopropyl

Bu = Butyl

i-Bu = Isobutyl

t-Bu = *tert*-butyl

Ph = Phenyl

Bn = Benzyl

Boc = *tert*-butyloxycarbonyl

AcOH or HOAc = acetic acid

$AlCl_3$ = aluminum chloride

CH_2Cl_2 = Dichloromethane

CH_3CN or CAN = Acetonitrile

$CDCl_3$ = deutero-chloroform

$CHCl_3$ = Chloroform

mCPBA or m-CPBA = *meta*-chloroperbenzoic acid

Cs_2CO_3 = cesium carbonate

DCM = Dichloromethane

DEA = Diethylamine

DIC = Diisopropylcarbodiimide

dil = dilute

DIPEA or Hunig's base = Diisopropylethylamine

DME = 1,2-dimethyoxyethane

DMF = Dimethylformamide

DMSO = dimethyl sulfoxide

cDNA = complimentary DNA

EDC = *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide

EDTA = ethylenediaminetetraacetic acid

Et_3N or TEA = Triethylamine

EtOAc = ethyl acetate

Et_2O = diethyl ether

EtOH = Ethanol

eq = equivalents

HCl = hydrochloric acid

HOBt = 1-hydroxybenzotriazole

HAUT = (2-(7-Aza-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate)

H_2SO_4 = sulfuric acid

K_2CO_3 = potassium carbonate

KOAc = potassium acetate

K_3PO_4 = potassium phosphate

LG = leaving group

LiOH = lithium hydroxide

MeOH = Methanol

min = minute or minutes

$MgSO_4$ = magnesium sulfate

MsOH or MSA = methylsulfonic acid

NaCl = sodium chloride

NaH = sodium hydride

$NaHCO_3$ = sodium bicarbonate

Na_2CO_3 = sodium carbonate

NaOH = sodium hydroxide

Na_2SO_3 = sodium sulfite

Na_2SO_4 = sodium sulfate

NH_3 = Ammonia

NH_4Cl = ammonium chloride

NH_4OH = ammonium hydroxide

$Pd(OAc)_2$ = palladium(II) acetate

Pd/C = palladium on carbon

$Pd(dppf)Cl_2$ = [1,1′-bis(diphenylphosphino)-ferrocene]dichloropalladium(II)

Ph_3PCl_2 = triphenylphosphine dichloride

$Pd(TRIPHENYLPHOSPHINE)_2Cl_2$ = Bis(triphenylphosphine)palladium(II)chloride

PG = protecting group

$POCl_3$ = phosphorus oxychloride

i-PrOH or IPA = Isopropanol

PS = Polystyrene

PyBOP = (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate

PyBrop = Bromo-tris-pyrrolidino phosphoniumhexafluorophosphate

SiO_2 = silica oxide

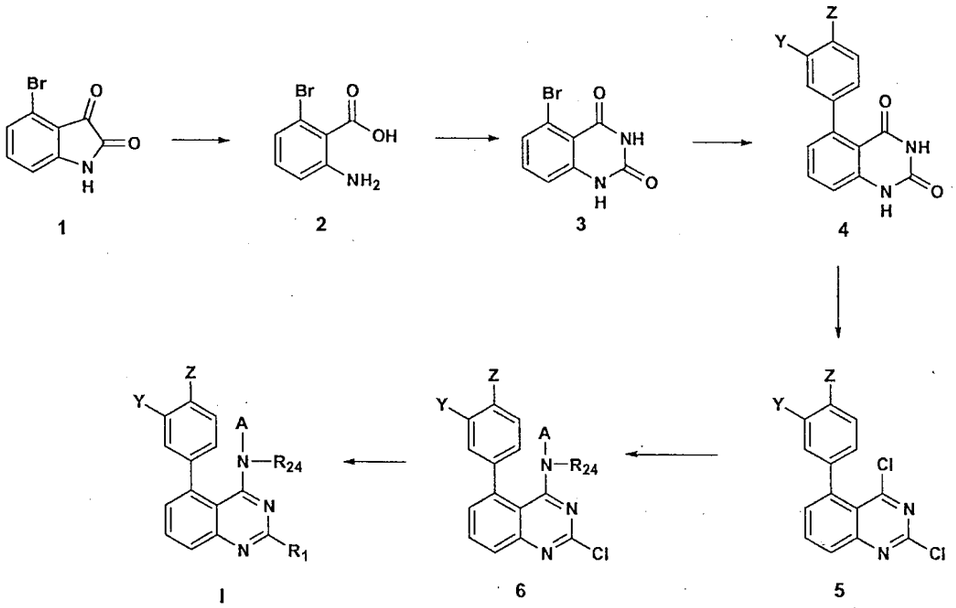
$SnCl_2$ = tin(II) chloride

TFA = trifluoroacetic acid

THF = Tetrahydrofuran

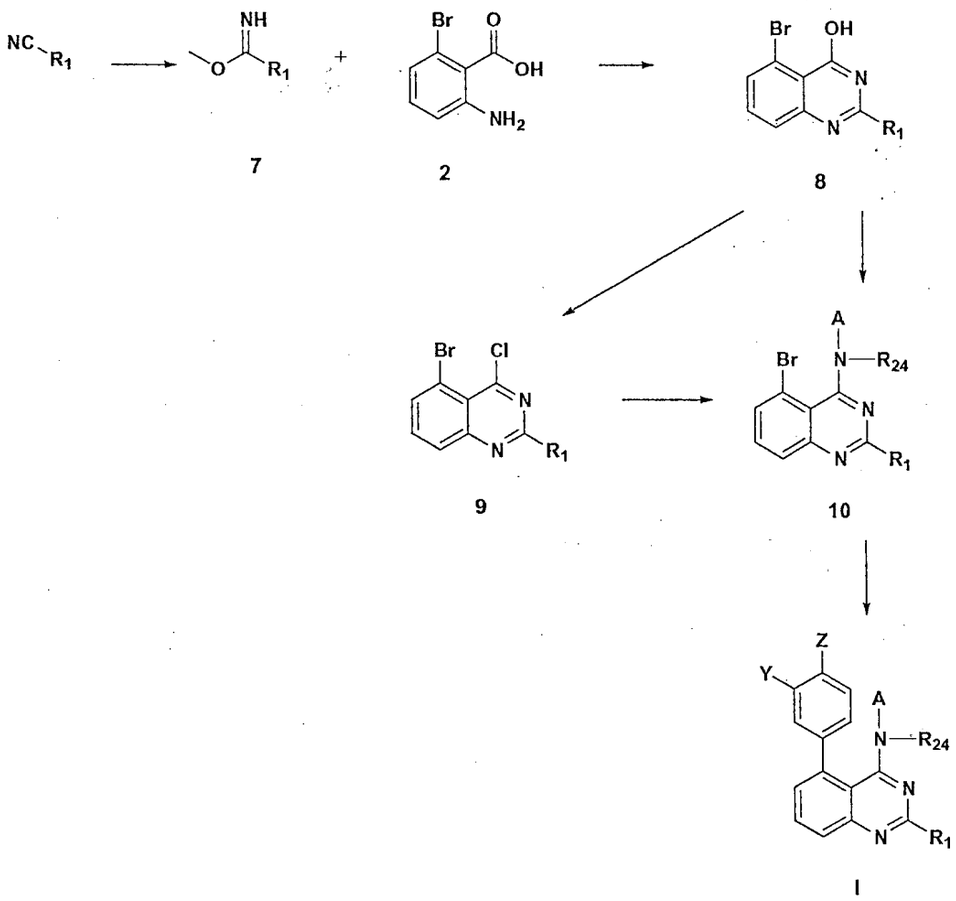
TOSMIC = Toluenesulfonylmethyl isocyanide

Scheme 1



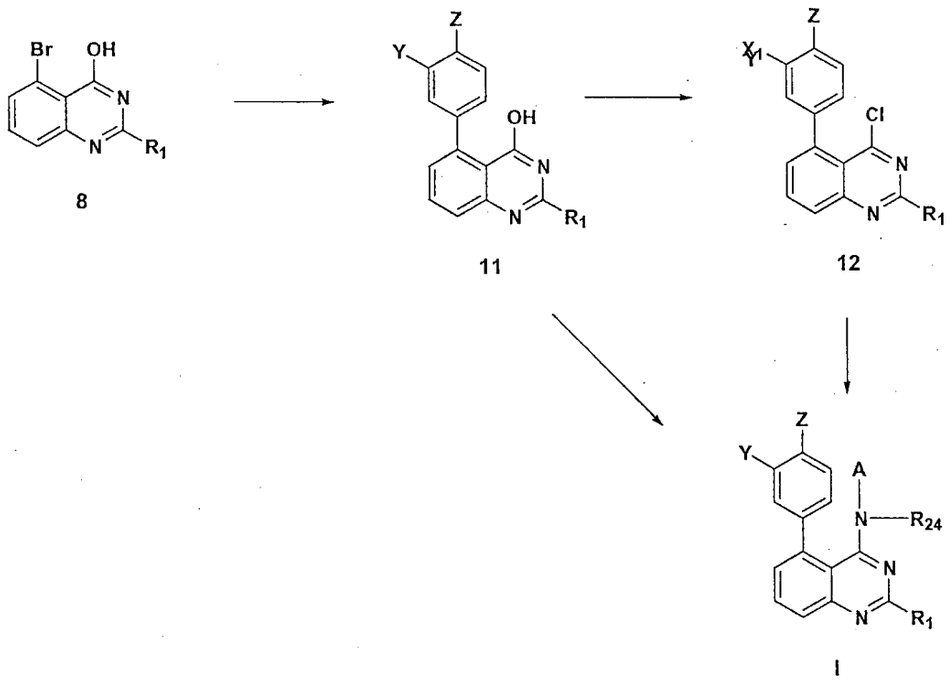
[0087] Compounds of formula I may be synthesized according to Scheme 1. Commercially available 4-bromoindoline-2,3-dione may be hydrolyzed to 2-amino-6-bromobenzamide followed by condensation with sodium isocyanate to form 5-bromoquinazoline-2,4(1H,3H)-dione. The protocols include, but are not limited to, palladium mediated cross coupling between 5-bromoquinazoline-2,4(1H,3H)-dione and the aryl boronic acid or ester to form the intermediate 5-substituted quinazoline-2,4(1H, 3H)-dione. Conversion to the corresponding dichloro quinazoline and sequential displacement at the 4- position followed by transition metal mediated cross coupling or displacement of the C_2 chloride forms compounds I as described.

Scheme 2



[0088] Alternatively, compounds of formula I may also be synthesized according to Scheme 2. Formation of the methyl-carbimidate from the corresponding nitrile and subsequent condensation with 2-amino-6-bromobenzamide provides compounds of formula **8**. Subsequent conversion of **8** to 4-chloroquinazoline intermediate **9** and displacement of the chloride provides 5-bromoquinazoline **10.** Compounds of formula **10** may be obtained directly from **8** utilizing coupling reagents, for example but not limited to, PyBOP in suitable solvents. The protocols include but are not limited to palladium mediated cross coupling between quinazoline **10** and a suitable aryl boronic acid or ester to obtain compounds of formula I.

Scheme 3



[0089] Alternatively, compounds of formula **I** may also be synthesized according to Scheme 3. Compounds of formula **8** may be subjected to cross coupling conditions, for example, but not limited to palladium mediated cross coupling of aryl boronic acids or esters, followed by subsequent conversion to the quinazoline intermediate **12** and displacement of the C_4 chloro group to obtain compounds of Formula **I**.

[0090] It should be recognized that the above schemes are only illustrations of some general synthetic routes to prepare compounds of the present invention. The experimental details for the synthesis of various specific examples of the present invention will be further described in the examples set forth below. Additional functional group manipulations of compounds obtained in the above schemes using methods known in the art should provide additional compounds of this invention.

EXAMPLES

[0091] The following examples are offered to illustrate, but not limit, some of the preferred embodiments of the present invention and are not meant to be limiting of the scope of the invention. Abbreviations and chemical symbols have their usual and customary meanings unless otherwise indicated. Unless otherwise indicated, the

compounds described herein have been prepared, isolated and characterized using the schemes and other methods disclosed herein or may be prepared using the same.

General Methods

[0092] The following methods were used in the working Examples, except where noted otherwise.

[0093] Analytical HPLC and HPLC/MS Methods Employed in Characterization of the examples are as follows:

[0094] Reverse phase analytical HPLC/MS was performed on Shimadzu LC10AS systems coupled with Waters ZMD Mass Spectrometers (methods A-C, E and F) or Waters AQUITY® system coupled with a Waters MICROMASS® ZQ Mass Spectrometer (method D). Chiral analytical LC was performed on a Berger Analytical SFC instrument (method G).

Method A:
Linear gradient of 0 to 100% B over 2 min, with 3 min hold at 100% B;
UV visualization at 220 nm;
Column: PHENOMENEX® Luna C18 4.6 x 30 mm;
Flow rate: 5 ml/min;
Solvent A: 0.1% trifluoroacetic acid, 90% water, 10% acetonitrile;
Solvent B: 0.1% trifluoroacetic acid, 90% acetonitrile, 10% water.

Method B:
Linear gradient of 0 to 100% B over 10 min, with 5 min hold at 100% B;
UV visualization at 220 nm;
Column: Xbridge phenyl 4.6 x 150 mm;
Flow rate: 1 ml/min;
Solvent A: 0.1% trifluoroacetic acid, 90% water, 10% acetonitrile;
Solvent B: 0.1% trifluoroacetic acid, 90% acetonitrile, 10% water.

Method C:

Linear gradient of 0 to 100% B over 4 min, with 1 min hold at 100% B;
UV visualization at 220 nm;
Column: PHENOMENEX® Luna C18 4.6 x 50 mm;
Flow rate: 4 ml/min;
Solvent A: 10mM ammonium acetate, 90% water, 10% methanol;
Solvent B: 10mM ammonium acetate, 90% methanol, 10% water.

Method D:
Linear gradient of 2 to 98% B over 1 min, with 0.5 min hold time at 98% B;
UV visualization at 220 nm;
Column: Waters BEH C18 2.1 x 50 mm;
Flow rate: 0.8 ml/min;
Solvent A: 0.05% TFA, 100% water;
Solvent B: 0.05% TFA, 100% ACN.

Method E:
Linear gradient of 0 to 100% B over 4 min, with 1 min hold time at 100% B;
UV visualization at 220 nm;
Column: Ascentis Express 4.6 x 50 C18 at 45 °C;
Flow rate: 4 ml/min;
Solvent A: 10 mM ammonium acetate, 5% ACN, 95% water;
Solvent B: 10 mM ammonium acetate, 95% ACN, 5% water.

Method F:
Linear gradient of 0 to 100% B over 8 min, with 1 min hold at 100% B;
UV visualization at 220 nm;
Column: PHENOMENEX® Luna C18 4.6 x 75 mm;
Flow rate: 2.5 ml/min;
Solvent A: 10mM ammonium acetate, 90% water, 10% methanol;
Solvent B: 10mM ammonium acetate, 90% methanol, 10% water.

Method G:

Isocratic 80/20 CO_2/MeOH containing 0.1% DEA;
UV visualization at 220 nm;
Column: CHIRALPAK® AC, 250 x 4.6 mm, 10 uM;
Flow rate: 3.0 ml/min.

[0095] Preparative HPLC methods employed in the purification of the examples are as follows:

Method H:
Linear gradient of 0 to 100% B over 10 min, with 5 min hold time at 100% B;
Shimadzu LC-8A binary pumps;
Waters ZQ mass spectrometer using Waters Masslynx 4.0 SP4 MS software;
UV visualization at 220 nm;
Column: Waters SunFire 19 x 100 mm 5 um C18;
Flow rate: 20 ml/min;
Peak collection triggered by mass spectrometry;
Solvent A: 0.1% TFA, 10% ACN, 90% water;
Solvent B: 0.1% TFA, 90% ACN, 10% water.

Method I:
Linear gradient of 20 to 100% B over 10 min, with 5 min hold time at 100% B;
Shimadzu LC-8A binary pumps;
Shimadzu SPD-20A UV detector;
UV visualization at 220 nm;
Column: PHENOMENEX® Luna AXIA 21.1 x 100 mm 5 um C18;
Flow rate: 20 ml/min;
Peak collection triggered by UV absorbance;
Solvent A: 0.1% TFA, 10% MeOH, 90% water;
Solvent B: 0.1% TFA, 90% MeOH, 10% water.

Method J:
Linear gradient of 20 to 100% B over 10 min, with 2 min hold time at 100% B;

Shimadzu LC-8A binary pumps;
Shimadzu SPD-10A UV detector;
UV visualization at 220 nm;
Column: PHENOMENEX® Luna AXIA 21.1 x 100 mm 5 um C18;
Flow rate: 20 ml/min;
Peak collection triggered by UV absorbance;
Solvent A: 0.1% TFA, 10% ACN, 90% water;
Solvent B: 0.1% TFA, 90% ACN, 10% water.

Method K:
Isocratic 80/20 CO_2/CH_3OH containing 0.1% DEA;
Berger Multigram II SFC instrument;
UV visualization at 220 nm;
Column: CHIRALPAK® AD-H 250 x 21 cm ID, 5 uM;
Flow rate: 65 ml/min;
Peak collection triggered by UV absorbance.

[0096] Additional Analytical HPLC and HPLC/MS Methods Employed in Characterization of Examples are as follows:

Method L:
Solvent A-5% ACN, 95% water, 10 mM NH_4OAc;
Solvent B-95% ACN, 5% Water, 10 mM NH_4OAc;
Flow rate: 4.0 ml/min;
Column: Ascentis Express C18 (4.6 X 50 cm) mm, 2.7um;
Time (min): 0-4.0 gradient %B: 0-100.

Method M:
Linear gradient of 0 to 100% B over 2 min;
UV visualization at 220 nm;
Column: PHENOMENEX® Luna C18 4.6 x 30 mm;
Flow rate: 5 mL/min;

Solvent A: 0.1% trifluoroacetic acid, 90% water, 10% methanol;
Solvent B: 0.1% trifluoroacetic acid, 90% methanol, 10% water.

Method N:
Linear gradient of 0 to 5% B over 0.25 min then 5 to 100% B up to 2 min with 0.5 min hold at 100% B;
UV visualization at 220 nm;
Column: BEH C18 50 x 2.1 mm - 1.7 µm;
Flow rate: 0.6 mL/min;
Solvent A: 0.1% formic acid, 95% water, 5% acetonitrile;
Solvent B: 0.1% formic acid, 95% acetonitrile, 5% water.

Method O:
Linear gradient of 0 to 100% B over 2 min;
UV visualization at 220 nm;
Column: CHROMOLITH® SpeedROD C18 4.6 x 30 mm;
Flow rate: 5 mL/min;
Solvent A: 0.1% trifluoroacetic acid, 90% water, 10% methanol;
Solvent B: 0.1% trifluoroacetic acid, 90% methanol, 10% water.

Method P:
Linear gradient of 40 to 95% B over 3 min with 3 min hold at 95% B;
UV visualization at 220 nm;
Column: Atlantis dC18 C18 50 x 4.6 mm - 5 µm;
Flow rate: 1.5 mL/min;
Solvent A: 0.1% formic acid in water;
Solvent B: acetonitrile.

Method Q:
Linear gradient of 0 to 100% B over 2 min;
UV visualization at 220 nm;
Column: PHENOMENEX® Luna C18 4.6 x 30 mm;

Flow rate: 5 mL/min;
Solvent A: 10mM ammonium acetate, 90% water, 10% methanol;
Solvent B: 10mM ammonium acetate, 90% methanol, 10% water.

Method R:
Linear gradient of 30 to 95% B over 3 min with 1 min hold at 95% B;
UV visualization at 220 nm;
Column: Atlantis dC18 C18 50 x 4.6 mm - 5 µm;
Flow rate: 1 mL/min;
Solvent A: 10mM ammonium acetate in water;
Solvent B: acetonitrile.

Method S:
Linear gradient of 40 to 95% B over 3 min with 1 min hold at 95% B;
UV visualization at 220 nm;
Column: Atlantis dC18 C18 50 x 4.6 mm - 5 µm;
Flow rate: 1.5 mL/min;
Solvent A: 10mM ammonium acetate in water;
Solvent B: acetonitrile.

Method T:
Linear gradient of 0 to 100% B over 2 min
Agilent 1200 series systems coupled with DADetector using Agilent chemstation & using Chemstation B.04.01 (482) software, with ESI ionization source in Positive mode only.
UV visualization at 220 nm;
Column: Agilent Zorbax SB C18 4.6 x 50 mm 5 um
Gradient Programme: Time (min)/%B: 0/0,2/100,3/0.
Flow rate: 5.0 ml/min;
Buffer: 0.1% Trifluoroacetic acid in water.
Mobile Phase A: Buffer: Methanol :90:10
Mobile Phase B: Buffer: Methanol :10:90

Method U:

Linear gradient of 0 to 100% B over 2 min;

UV visualization at 220 nm;

Column: Chromolith SpeedROD C18 4.6 x 30 mm;

Flow rate: 5 mL/min;

Solvent A: 0.1% trifluoroacetic acid, 90% water, 10% methanol;

Solvent B: 0.1% trifluoroacetic acid, 90% methanol, 10% water.

Method V:

Linear gradient of 0 to 100% B over 1.5 min, with 1.7 min hold at 100% B;

Agilent 1200 series systems coupled with DADetector using Agilent chemstation & using Chemstation B.04.01 (482) software; with ESI ionization source in both Positive & Negative mode.

UV visualization at 220 nm;

Column: Waters Xbridge Phenyl 4.6 x 30 mm 3.5 um

Gradient Programme: Time (min)/%B: 0/0,1.5/100,3.2/100,3.6/0,4.0/0

Flow rate: 1.8 ml/min;

Buffer: 10mM Ammonium Formate in water.

Mobile Phase A: Buffer: Acetonitrile: 98:02

Mobile Phase B: Buffer: Acetonitrile: 02:98

Method W:

Linear gradient of 0 to 100% B over 2.50min, with 0.5min hold at 100% B;

Agilent 1200 series systems coupled with DADetector using Agilent chemstation & Chemstation B.04.01 (482) software with Multi mode ionization source in both Positive & Negative mode.

UV visualization at 220 nm;

Column: Merck Puroshpere @ Star RP-18 4 x 5 mm, 3u

Gradient Programme: Time (min)/%B: 0/0,2.0/100,2.5/100,3.0/0,3.5/0

Flow rate: 2.5ml/min;

Buffer: 20mM Ammonium Acetate in water.

Mobile Phase A: Buffer: Acetonitrile: 90:10

Mobile Phase B: Buffer: Acetonitrile: 10:90

Method X:

Linear gradient of 0 to 100% B over 2 min;

UV visualization at 220 nm;

Column: Phenomenex Luna C18 4.6 x 30 mm;

Flow rate: 5 mL/min;

Solvent A: 10mM ammonium acetate, 90% water, 10% methanol;

Solvent B: 10mM ammonium acetate, 90% methanol, 10% water.

Method Y:

Reverse phase analytical HPLC/MS was performed on Agilent 1200 series systems coupled with DADetector, Ion-Trap 6330 Mass Spectrometer, 1200 ELSD (Agilent) using Agilent chemstation & Brooker 4.0 Build 234 software in both Positive & Negative mode.

Linear gradient of 0 to 100% B over 1.2min, with 1.8min hold at 100% B;

Agilent 1200 series systems coupled with DADetector

UV visualization at 220 nm;

Column: Ascentis Express C18 2.1 x 50 mm, 2.7u

Gradient Programme: Time (min)/%B: 0/0,1.2/100,3.0/100,3.4/0,4.0/0

Flow rate: 1.0ml/min;

Buffer: 10mM Ammonium Formate in water.

Mobile Phase A: Buffer: Acetonitrile: 98:02

Mobile Phase B: Buffer: Acetonitrile: 02:98

Method Z:

Reverse phase analytical HPLC/MS was performed on Agilent 1200 series systems coupled with DADetector, Ion-Trap 6330 Mass Spectrometer, 1200 ELSD (Agilent) using Agilent chemstation & Brooker 4.0 Build 234 software in both Positive & Negative mode.

Linear gradient of 0 to 100% B over 1.2min, with 1.8min hold at 100% B;

Agilent 1200 series systems coupled with DADetector

UV visualization at 220 nm;

Column: Zorbax AQ C18 4.6 x 50 mm, 3.5u

Gradient Programme: Time (min)/%B: 0/2,1.5/20,4.0/95,4.5/2,6/2

Flow rate: 1.0ml/min;

Buffer: 0.1% Formic Acid in water.

Mobile Phase A: 0.1% Formic Acid in water.

Mobile Phase B: Acetonitrile.

Method Z1:

Method info:

A: Water:ACN (95:5); 10mM ammonium acetate

B: Water:ACN (5:95); 10mM ammonium acetate

Flow: 4 ml/min

Temp: 45°C

Column: Ascentis Express C18 (50x4.6), 2.7µm

Time (min): 0---4

Method A1:

Linear gradient of 10 to 100% B over 12 min, with 3 min hold at 100% B;

Gradient Programme: T/%B: 0/10, 12/100, 15/100, 18/10, 23/10

UV visualization at 220 & 254 nm;

Waters Sunfire C18 (4.6 x 150 mm, 3.5u)

Flow rate: 1 ml/min

Buffer: 0.05% Trifluoroacetic acid in water pH adjusted to 2.5 with dil Ammonia

Mobile Phase A: Buffer: Acetonitrile: 95:05

Mobile Phase B: Buffer: Acetonitrile: 05:95

Method A2:

Linear gradient of 10 to 100% B over 12 min, with 3 min hold at 100% B;

Gradient Programme: T/%B: 0/10, 12/100, 15/100, 18/10, 23/10

UV visualization at 220 & 254 nm;
Waters Xbridge Phenyl (4.6 x 150 mm, 3.5u)
Flow rate: 1 ml/min
Buffer: 0.05% Trifluoroacetic acid in water pH adjusted to 2.5 with dil Ammonia
Mobile Phase A: Buffer: Acetonitrile: 95:05
Mobile Phase B: Buffer: Acetonitrile: 05:95

Method A3:
Linear gradient of 10 to 100% B over 12 min, with 8 min hold at 100% B;
Gradient Programme: Time (min)/%B: 0/10, 12/100, 20/100, 23/10, 26/10
UV visualization at 220 & 254 nm;
Waters Xbridge Phenyl (4.6 x 150 mm, 3.5u)
Flow rate: 1.0 ml/min;
Mobile Phase A: 10mM Ammonium Bicarbonate in water pH adjusted to 9.5 with dil Ammonia
Mobile Phase B: Methanol

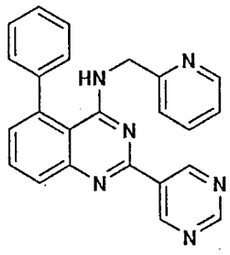
Method A4:
Linear gradient of 0 to 100% B over 10 min, with 5 min hold at 100% B;
UV visualization at 220 nm;
Column: X-bridge phenyl 4.6 x 150 mm;
Flow rate: 1 ml/min;
Solvent A: 0.1% trifluoroacetic acid, 90% water, 10% acetonitrile;
Solvent B: 0.1% trifluoroacetic acid, 90% acetonitrile, 10% water.

[0097] ^{1}H NMR spectra were obtained with Bruker or JEOL FOURIER® transform spectrometers operating at frequencies as follows: ^{1}H NMR: 400 MHz (Bruker or JEOL) or 500MHz (JEOL). ^{13}C NMR: 100 MHz (Bruker or JEOL). Spectra data are reported in the format: chemical shift (multiplicity, coupling constants, and number of hydrogens). Chemical shifts are specified in ppm downfield of a tetramethylsilane internal standard (δ units, tetramethylsilane = 0 ppm) and/or referenced to solvent peaks, which in ^{1}H NMR spectra appear at 2.49 ppm for

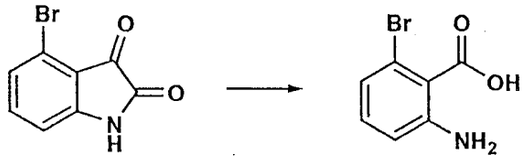
CD_2HSOCD_3, 3.30 ppm for CD_2HOD, and 7.24 ppm for $CHCl_3$, and which in ^{13}C NMR spectra appear at 39.7 ppm for CD_3SOCD_3, 49.0 ppm for CD_3OD, and 77.0 ppm for $CDCl_3$. All ^{13}C NMR spectra were proton decoupled.

EXAMPLE 1

5-Phenyl-N-(pyridin-2-ylmethyl)-2-(pyrimidin-5-yl)quinazolin-4-amine

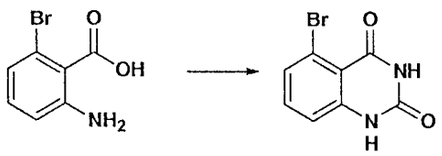


Step 1. Preparation of 2-amino-6-bromobenzoic acid



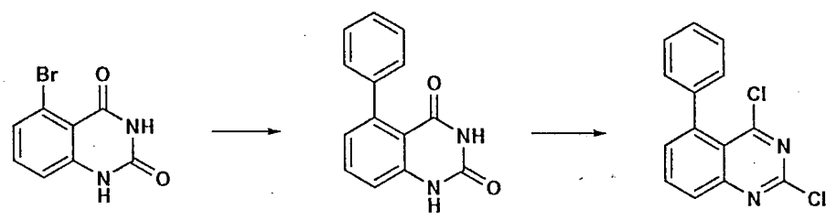
[0098] To 4-bromoindoline-2,3-dione (8.94 g, 39.6 mmol) was added 1.0 M sodium hydroxide (40 mL, 120 mmol) to give a dark brown mixture. The mixture was heated to 80 °C then 20% hydrogen peroxide (9 mL, 88 mmol) was added slowly over 15 min (caution: a strong exotherm was observed upon reagent addition). The mixture was then stirred at 80 °C for 1h. After this time, the mixture was cooled in an ice bath to ~10 °C and then concentrated to a residue. HCl was added cautiously to the residue until the pH of the mixture was 4-5. Once at the prescribed pH, the mixture was then concentrated to dryness and MeOH (150 ml) was added. The resulting suspension stirred for 15 min and then filtered. The filtrate was concentrated to dryness and dried under vacuum for 14 h to yield 2-amino-6-bromobenzoic acid (9.18 g) as a brown solid. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 6.72 (1 H, t, *J*=7.91 Hz), 6.60 (1 H, dd, *J*=7.78, 1.00 Hz), 6.52 (1 H, dd, *J*=7.91, 1.13 Hz). LCMS Method D: retention time 0.68 min, [M+1] 200.0.

Step 2. Preparation of 5-bromoquinazoline-2,4(1H,3H)-dione



[0099] 2-Amino-6-bromobenzoic acid (2.97 g, 13.7 mmol) was suspended in a mixture of water (100 mL) and acetic acid (1.5 mL) at 35 °C then a suspension of sodium cyanate (2.23 g, 34.4 mmol) in 10 mL of water was added slowly to the mixture. Upon completion of addition, the resulting mixture was stirred at 35 °C for 30 minutes and then sodium hydroxide (24.7 g, 619 mmol) pellets were slowly added to the mixture to yield a thick precipitate. The mixture was cooled to 5 °C in an ice bath and the pH of the suspension was adjusted to 4 using concentrated HCl. Once at the prescribed pH, the suspension was filtered and the solid was washed with water and dried under vacuum while heating at 100 °C to give 5-bromo-1H-quinazoline-2,4-dione (1.91 g) as a brown solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 11.30 (1 H, br. s.), 11.26 (1 H, br. s.), 7.43 - 7.48 (1 H, m), 7.40 (1 H, dd, *J*=7.78, 1.25 Hz), 7.16 (1 H, dd, *J*=7.91, 1.13 Hz).

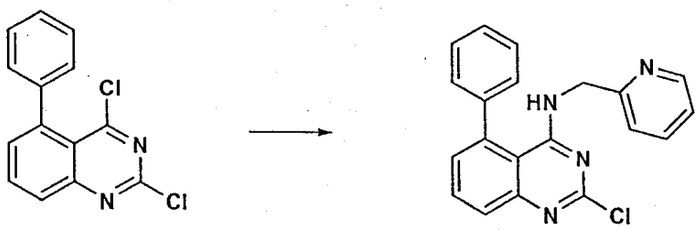
Step 3. Preparation of 2,4-dichloro-5-phenylquinazoline



[00100] See *J. Med. Chem.*, 50(7):1675 (2007), 76759-011. To a mixture of 5-bromoquinazoline-2,4(1H,3H)-dione (900 mg, 3.73 mmol) and $Pd(Ph_3P)_4$ (216 mg, 0.187 mmol) in DME (90 mL) was added phenylboronic acid (683 mg, 5.60 mmol) followed by a solution of sodium bicarbonate (941 mg, 11.2 mmol) in water (30 mL) and the reaction heated at reflux for 40 h. At the conclusion of this period, the organic solvent was removed under reduced pressure. The resulting mixture was filtered and the solid washed with water. The solid was concentrated under reduced pressure from MeOH/DCM to remove the water to yield 5-phenylquinazoline-2,4(1H,3H)-dione as an off-white solid. The 5-phenylquinazoline-2,4(1H,3H)-dione (9.64 g, 40.4 mmol) was added to $POCl_3$ (75 mL, 810 mmol) followed by $PhN(CH_3)_2$

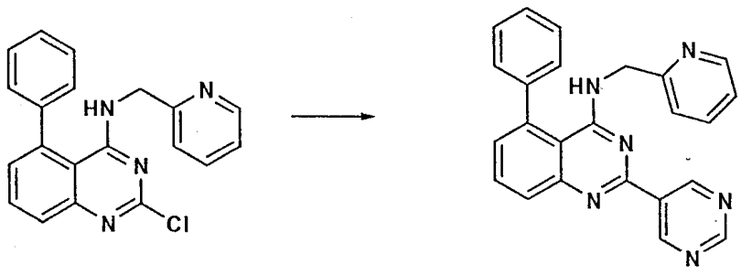
(10.3 mL, 81.0 mmol). Upon completion of addition, the reaction mixture was heated to reflux (105 °C) where it was stirred for 2 hours. After this time, the reaction mixture was allowed to cool to ambient temperature. Once at the prescribed temperature, the reaction mixture was concentrated under reduced pressure, diluted with DCM and then quenched by the addition of cold 1M K_3PO_4 solution. The organic layer was separated and the aqueous layer was extracted twice with DCM. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure to yield a residue. The residue was purified by ISCO chromatography (330 g column) using hexanes/EtOAc (0-25% over 20 min, flow rate 100 mL/min) to give 2,4-dichloro-5-phenylquinazoline (7.11 g, 63.9 % yield) as a yellow solid. ^{1}H NMR (400 MHz, chloroform-d) ppm 8.04 (1 H, m) 7.96 (1 H, m) 7.59 (1 H, dd, *J*=7.28, 1.25 Hz) 7.45 (3 H, dd, *J*=5.02, 1.76 Hz) 7.32 (2 H, m).

Step 4. Preparation of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine



[00101] 2,4-Dichloro-5-phenylquinazoline (1.38 g, 5.03 mmol) was dissolved in THF (80 mL) and triethylamine (1.33 mL, 9.56 mmol) was added dropwise. The mixture was stirred for 5 min at room temperature and then pyridin-2-ylmethanamine (0.57 mL, 5.53 mmol) was added dropwise. The resulting mixture was stirred at ambient temperature for 14 hours. After this time, the mixture was filtered through a medium porosity glass frit, concentrated to dryness under reduced pressure and then purified by ISCO flash column chromatography (80 g silica gel column) eluting with 0-100% ethyl acetate/hexanes over 30 min to provide 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (1.32 g, 75 %). LCMS Method A [M+1] observed 347.1. HPLC Method B: Purity 99.1% retention time 6.66 min. ^{1}H NMR (400 MHz, chloroform-d) δ ppm 8.16 (1 H, d, *J*=4.77 Hz), 7.79 (1 H, d, *J*=7.28 Hz), 7.70 (1 H, t, *J*=7.78 Hz), 7.59 (1 H, dt, *J*=7.53, 1.51 Hz), 7.40 - 7.55 (5 H, m), 7.08 - 7.25 (4 H, m), 4.66 (2 H, d, *J*=4.02 Hz).

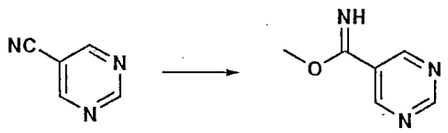
Step 5. Example 1



[00102] 2-Chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (225 mg, 0.649 mmol), pyrimidin-5-ylboronic acid (121 mg, 0.973 mmol), and bis (triphenylphosphine)palladium (II) chloride (23 mg, 0.032 mmol) were combined in a microwave tube which was sealed, evacuated and then backfilled with argon. Under argon, previously degassed dioxane (1 mL) and a sodium carbonate (0.33 mL, 0.330 mmol) in water (0.33 mL) solution were added to the reaction mixture. The resulting mixture was heated under microwave irradiation to 100 °C where it was maintained for 60 min. After this time, additional pyrimidin-5-ylboronic acid (91 mg, 0.7773 mmol) and bis (triphenylphosphine)palladium (II) chloride (17 mg, 0.024 mmol) were added. Upon completion of addition, the resulting mixture was heated under microwave irradiation at 100 °C for 40 min and then allowed to cool to room temperature where it stirred for 14 h. At the conclusion of this period, the reaction mixture was diluted with 50 mL each of water and ethyl acetate. The organic layer was separated and the aqueous portion was extracted with ethyl acetate. The combined organic portions were washed with 50 mL of brine, dried over Na_2SO_4, decanted and concentrated under reduced pressure to yield a crude residue. The crude residue was purified by ISCO (40 g silica gel column) eluting with 0-5% MeOH over 15 min and then 5% MeOH for 10 min to yield Example 1 (212 mg, 84 %). ^{1}H NMR (400 MHz, $CDCl_3$) ppm 4.74 (d, *J*=4.27 Hz, 2 H) 6.73 - 6.81 (m, 1 H) 7.09 - 7.16 (m, 2 H) 7.25 - 7.29 (m, 1 H) 7.44 - 7.52 (m, 5 H) 7.58 (dt, *J*=7.72, 1.88 Hz, 1 H) 7.73 (dd, *J*=8.28, 7.28 Hz, 1 H) 7.93 (dd, *J*=8.28, 1.25 Hz, 1 H) 8.23 - 8.26 (m, 1 H) 9.29 (s, 1 H) 9.78 (s, 2 H). LCMS Method D: retention time 0.76min, [M+1] = 391; HPLC Method B: purity 99%, retention time 5.6 min.

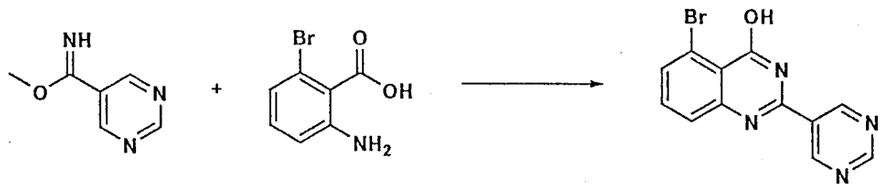
[00103] Alternatively, Example 1 can be synthesized as follows:

Step 1. Preparation of methyl pyrimidine-5-carbimidate



[00104] To a stirred suspension of 5-cyanopyrimidine (5.0 g, 47 mmol) in methanol (50 mL) was added 25% by weight sodium methoxide in methanol (1.2 g, 23 mmol). The mixture was stirred at room temperature for 17 h under nitrogen atmosphere and then acetic acid (2.72 ml, 47 mmol) was added dropwise. The resulting mixture was stirred for 4 h and then evaporated under reduced pressure to remove methanol and yield a residue. The residue was dissolved in ether (150 mL) and the solids were removed by filtration. The filtrate was concentrated under reduced pressure to yield methyl pyrimidine-5-carbimidate (4.9 g, 75% yield). The crude product was used without further purification. ^{1}H NMR (400 MHz, DMSO-d_6, δ): 3.83 (s, 3H); 9.18 (s, 2H); 9.30 (s, 1H); 9.54 (s, 1H). ES-MS: [M^++1] = 138.

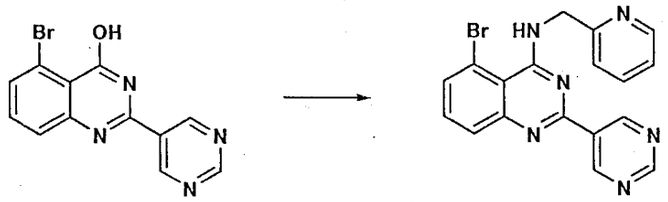
Step 2. Preparation of 5-bromo-2-(pyrimidin-5-yl)quinazolin-4-ol



[00105] To a stirred suspension of methyl pyrimidine-5-carbimidate (2.00 g, 14.5 mmol) in methanol (20 mL) was added 2-amino-6-bromobenzoic acid (3.1 g, 14.5 mmol). The mixture was heated to reflux where it stirred for 16 h under the nitrogen atmosphere. At the conclusion of this period, acetic acid (2.72 ml, 47 mmol) was added drop wise. Upon completion of addition, methanol was evaporated under reduced pressure to yield a residue. The residue was triturated with ether (100 mL), ethyl acetate (50 mL) and the resulting solid was dried to yield 5-bromo-2-(pyrimidin-5-yl)quinazolin-4-ol (1.2 g, 27%) as an off-white solid. The crude product was used without further purification. ^{1}H NMR (400 MHz, DMSO-d_6, δ): 7.64 (dd, *J*

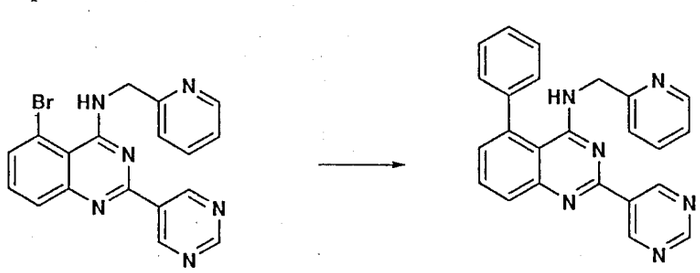
= 7.2Hz, 8.4Hz, 1H); 7.73-7.75 (m, 2H); 9.35 (s, 1H); 9.46 (s, 2H); 12.9 (br s, 1H). ES-MS: $[M^+ +1] = 303$ and $[M^+ +3] = 305$.

Step 3. Preparation of 5-bromo-N-(pyridin-2-ylmethyl)-2-(pyrimidin-5-yl)quinazolin-4-amine



[00106] To a stirred suspension of 5-bromo-2-(pyrimidin-5-yl)quinazolin-4-ol (2.0 g, 6.5 mmol) in DMF (20 mL) was added diisopropylethyl amine (3.4 ml, 19 mmol) followed by PyBroP (3.7 g, 7.9 mmol). After 5 min stirring at room temperature, 2-aminomethylpyridine (1.0 mL, 9.8 mmol) was added to the reaction. Upon completion of addition, the reaction mixture was warmed to 80 °C where it stirred for 2h (during which time reaction became a clear solution). At the conclusion of this period, the reaction mixture was quenched by the addition of cold water and then extracted into 50% ethyl acetate and hexane mixture (200 mL). The organic extracts were dried, concentrated, purified by column chromatography using ethyl acetate and hexanes as eluent to yield the crude produce. The crude product was further purified by trituration with ethyl acetate and hexane to yield 5-bromo-N-(pyridin-2-ylmethyl)-2-(pyrimidin-5-yl)quinazolin-4-amine (0.5g, 20% yield). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 5.07 (d, J = 4.4Hz, 2H); 7.26 (m, 1H); 7.41 (d, J = 7.6Hz, 1H); 7.53 (t, J = 8Hz, 1H); 7.71-7.73 (m, 2H); 7.86 (dd, J = 0.8Hz, 8.4Hz, 1H); 8.65 (d, J = 4Hz, 1H); 9.30 (s, 1H); 9.38 (br s, 1H); 9.75 (s, 2H). ES-MS: $[M^+ +1] = 393$ and $[M^+ +3] = 395$.

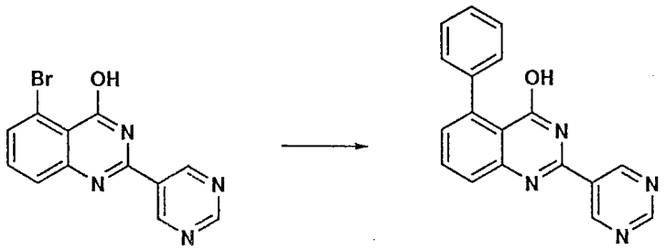
Step 4. Example 1



[00107] A stirred suspension of 5-bromo-N-(pyridin-2-ylmethyl)-2-(pyrimidin-5-yl)quinazolin-4-amine (1.0 g, 2.5 mmol), phenylboronic acid (0.46 g, 3.8 mmol) and potassium carbonate (1.0 g, 7.6 mmol) in dimethoxyethane-water (3-1, 10 mL) was degassed and charged with tetrakistriphenylphosphene palladium (0.14 g, 0.12 mmol). The reaction mixture was then heated to 90 °C where it stirred for 16 h under a nitrogen atmosphere. After this time, the reaction mixture was quenched with water (5 mL) and then extracted with ethyl acetate (3 x 25 mL). The combined organic extracts were dried and then concentrated to yield the crude product. The crude product was purified by preparative TLC using chloroform and methanol (95:5) as the solvent system to yield Example 1 (40 mg, 4% yield). ^{1}H NMR (400 MHz, DMSO-d_6, δ): 5.01 (d, J = 5.6Hz, 2H); 7.27 (t, J = 4.0Hz, 1H); 7.41-7.56 (m, 5H); 7.66-7.79 (m, 4H); 7.91 (d, J = 6.8Hz, 1H); 8.42 (d, J = 8Hz, 1H); 8.55 (d, J = 4.8Hz, 1H); 9.23 (s, 1H); 9.32 (t, J = 6Hz, 1H); 9.40 (s, 2H). LCMS Method O: retention time 1.67min, [M+1] = 391. HPLC Method B: purity 99%, retention time 8.5 min.

[00108] Example 1 can also be synthesized as follows:

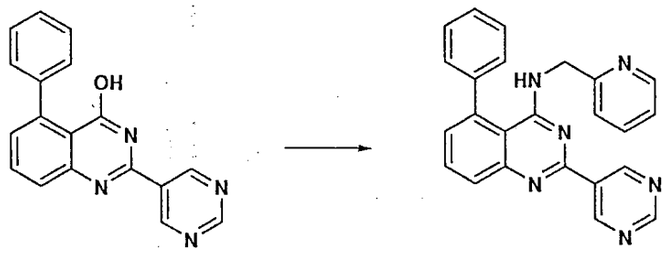
Step 1. Preparation of 5-phenyl-2-(pyrimidin-5-yl)quinazolin-4-ol



[00109] A stirred suspension of 5-bromo-2-(pyrimidin-5-yl)quinazolin-4-ol (2.0 g, 6.6 mmol), phenylboronic acid (1.2 g, 9.9 mmol) and a solution of potassium carbonate (2.6 g, 19.8 mmol) in dimethoxyethane and water (3:1, 15 mL) was degassed and charged with 1,1'-bis(diphenylphosphino)ferrocene palladium dichloride (0.24 g, 0.33 mmol). The reaction mixture was heated to 90 °C where it stirred for 24 h under nitrogen atmosphere. At the conclusion of this period, the reaction mixture was concentrated to yield the crude product. The crude product was purified by flash column chromatography on silica gel using 2 % methanol in dichloromethane as eluent to yield 5-phenyl-2-(pyrimidin-5-yl)quinazolin-4-ol (800

mg, 27 % yield). ^{1}H NMR (400 MHz, DMSO-d_6, δ): 7.29-7.40 (m, 6H); 7.79-7.87 (m, 4H); 9.37 (s, 1H); 9.45 (s, 2H); 12.59 (br s, 1H). LCMS Method O: retention time 1.68min, [M+1] = 301.

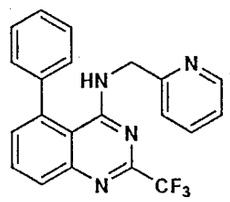
Step 2: Example 1



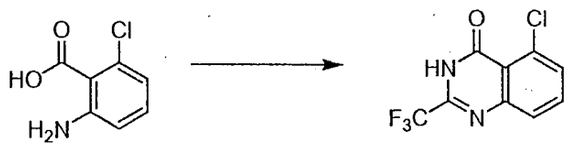
[00110] 5-Phenyl-2-(pyrimidin-5-yl)quinazolin-4-ol was subsequently converted to Example 1 utilizing the reagents and conditions described for the preparation of 5-bromo-N-(pyridin-2-ylmethyl)-2-(pyrimidin-5-yl)quinazolin-4-amine in step 3 above.

EXAMPLE 2

5-Phenyl-N-(pyridin-2-ylmethyl)-2-(trifluoromethyl)quinazolin-4-amine



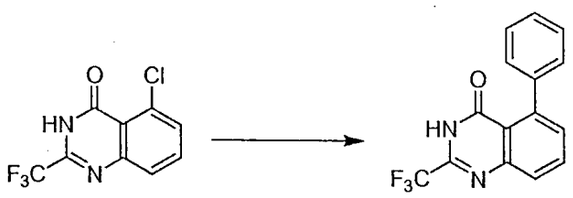
Step 1. Preparation of 5-chloro-2-(trifluoromethyl)quinazolin-4(3H)-one



[00111] See U.S. Patent No. 3,843,791. To a solution of 2-amino-6-chlorobenzoic acid (1.91 g, 11.13 mmol) in a mixture of chloroform (22 mL) and dry pyridine (1.5 mL) at 0°C was added trifluoroacetic anhydride (3.52 mL, 24.94 mmol). Upon completion of addition, the reaction mixture was heated to reflux where it stirred for 2h. After this time, the reaction mixture was cooled to room temperature and concentrated to yield a crude material. The crude material was dissolved in

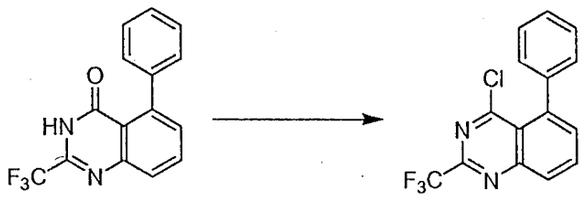
chloroform (22 mL), saturated with ammonia gas and then stirred for 30 min at room temperature. After this time, the mixture was concentrated and the resulting solid was washed with 1N HCl (2x20 mL) and diluted with ethyl acetate (100 mL) and water (100 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (100 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated to yield the crude product. The crude product was purified by flash chromatography on silica gel eluting with 2-15% ethyl acetate/hexanes to afford 5-chloro-2-(trifluoromethyl)quinazolin-4(3H)-one (1.3 g, 46%) as a white solid. ^1H NMR (400 MHz, chloroform-d) ppm 10.23 (1 H, br. s.), 7.71 - 7.82 (2 H, m), 7.64 (1 H, d, *J*=7.15 Hz). LCMS Method A: retention time 0.65 min [M+1] = 250.

Step 2. Preparation of 5-phenyl-2-(trifluoromethyl)quinazolin-4(3H)-one



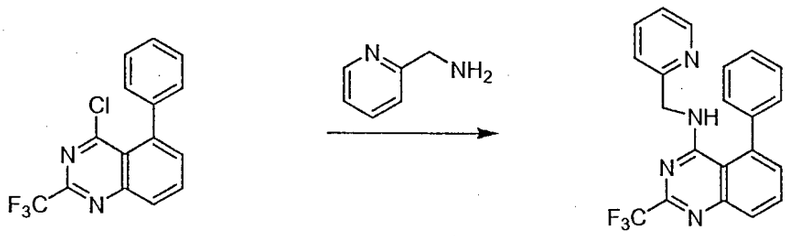
[00112] Palladium (II) acetate (19 mg, 0.085 mmol), potassium fluoride (498 mg, 8.57 mmol), 2-(di-*tert*-butylphosphino)biphenyl (51.1 mg, 0.171 mmol), and phenylboronic acid (522 mg, 4.27 mmol) were combined in a microwave vial under an argon atmosphere. A solution of 5-chloro-2-(trifluoromethyl)quinazolin-4(3H)-one (710 mg, 2.86 mmol) in dry THF (9 mL) was added and the mixture was heated in the microwave at 100°C for 30 min. After this time, the reaction mixture was diluted with ethyl acetate (50 mL) and washed with 1N NaOH (25 mL) and saturated NaCl (25 mL). The organic layer was separated, dried over sodium sulfate and then concentrated under reduced pressure to give the crude product (968 mg), which was used in the next step without further purification.

Step 3. Preparation of 4-chloro-5-phenyl-2-(trifluoromethyl)quinazoline



[00113] To the crude material from Step 2, Example 3, was added phosphorous oxychloride (2.86 mL, 307 mmol) and N,N-dimethylaniline (425 μL, 3.34 mmol). The reaction mixture was heated to 100°C where it stirred for 10 min. After this time, the reaction mixture was cooled to room temperature. Once at the prescribed temperature, the solvents were removed under reduced pressure to yield a residue, which was then dissolved in dichloromethane (20 mL). The dichloromethane solution was added to 50 mL of a 1.5 M KH_2PO_4 solution. Upon completion of addition, the dichloromethane was removed under reduced pressure and the aqueous layer was extracted with DCM (3x50 mL). The combined organic portions were dried over sodium sulfate and concentrated under reduced pressure to yield a second residue. The second residue was purified by flash chromatography on silica gel eluting with 100% DCM to yield 4-chloro-5-phenyl-2-(trifluoromethyl)quinazoline (612 mg, 59% yield) as a white solid. ^{1}H NMR (400 MHz, chloroform-d) ppm 8.27 (1 H, d, *J*=8.53 Hz), 8.07 (1 H, t, *J*=7.78 Hz), 7.75 (1 H, d, *J*=7.03 Hz), 7.42 - 7.54 (3 H, m), 7.29 - 7.38 (2 H, m). LCMS Method D: retention time 1.07 min [M+1] = 309.

Step 4. Example 2

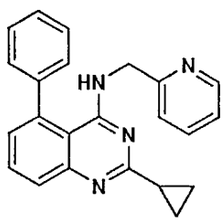


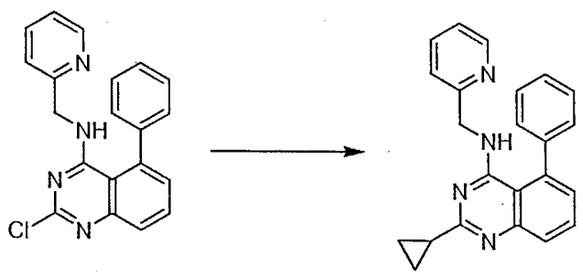
[00114] To a solution of 4-chloro-5-phenyl-2-(trifluoromethyl)quinazoline (200mg, 0.648 mmol) in THF (15 mL) was added triethylamine (0.172 mL, 1.231 mmol). Upon completion of addition, the reaction mixture was stirred and pyridin-2-ylmethanamine was added (0.080 mL, 0.777 mmol). The resulting reaction mixture was stirred at room temperature for 1h and then filtered. The filtrate was

concentrated under reduced pressure to yield a residue. The residue was purified by flash chromatography on silica gel eluting with 0-75% ethyl acetate/hexanes to yield Example 2 (217 mg, 88% yield) as a white solid. ^{1}H NMR (400 MHz, chloroform-d) ppm 8.20 (1 H, d, *J*=4.55 Hz), 7.99 (1 H, d, *J*=8.34 Hz), 7.78 (1 H, t, *J*=7.71 Hz), 7.59 (1 H, t, *J*=7.58 Hz), 7.42 - 7.54 (5 H, m), 7.35 (1 H, d, *J*=7.33 Hz), 7.03 - 7.22 (3 H, m), 4.69 (2 H, d, *J*=4.04 Hz). LCMS Method D: retention time 0.90 min [M+1] = 381.

EXAMPLE 3

2-Cyclopropyl-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine



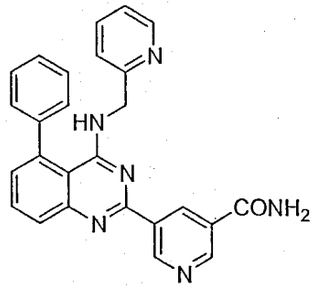


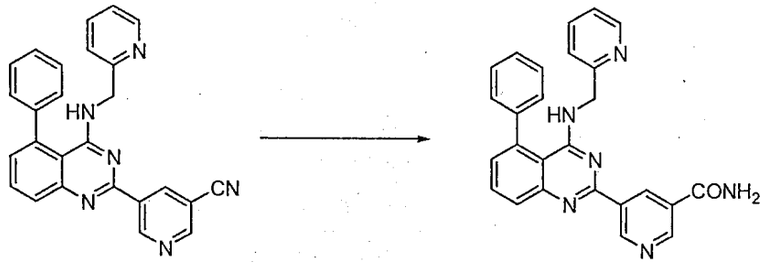
[00115] To a mixture of zinc bromide (64.9 mg, 0.288 mmol) and 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (5.89 mg, 7.21 µmol) was added anhydrous THF (0.3 mL). Upon completion of addition, the mixture was cooled to -78°C. Once at the prescribed temperature, cyclopropyl magnesium bromide (0.288 mL, 0.144 mmol) was added dropwise and the mixture was stirred at -78 °C for 15 min. At the conclusion of this period, a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (50 mg, 0.144 mmol) in anhydrous THF (1.5 mL) was added. The resulting mixture was stirred at -78 °C for 1h and then allowed to warm to room temperature where it stirred for 18h. After this time, the reaction mixture was diluted with saturated NH_4Cl (5

mL) and the aqueous layer extracted with ethyl acetate (3x20 mL). The organic portions were combined and washed with saturated NaCl, dried over sodium sulfate and concentrated under reduced pressure to yield the crude product. The crude product was purified by preparative HPLC (YMC Sunfire 5u C18 30x100 mm, Mobile Phase A: 10% MeOH - 90% H_2O - 0.1% TFA, Mobile Phase B: 90% MeOH - 10% H_2O - 0.1% TFA, 20-100% B over 10 min, 100% B for 2 min) to yield Example 3 (3.73 mg, 7% yield) as a pale yellow solid. ^{1}H NMR (400 MHz, chloroform-d) ppm 8.27 - 8.30 (1 H, m), 7.77 (1 H, dd, *J*=8.46, 0.88 Hz), 7.63 (1 H, dd, *J*=8.34, 7.07 Hz), 7.56 (1 H, td, *J*=7.71, 1.77 Hz), 7.41 - 7.48 (5 H, m), 7.04 - 7.15 (3 H, m), 6.30 (1 H, br. s.), 4.57 (2 H, d, *J*=4.55 Hz), 2.11 - 2.20 (1 H, m), 1.10 - 1.16 (2 H, m), 0.92 - 0.98 (2 H, m). LCMS Method D: retention time 0.76 min [M+1] = 353.

EXAMPLE 6

5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinamide



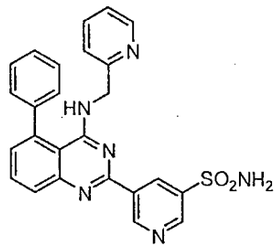


[00116] To a solution of 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinonitrile (prepared in a similar manner to the procedures described in Example 1, 200 mg, 0.48 mmol) in THF (5 mL) was slowly added a solution of sodium hydroxide (77 mg, 1.92 mmol) in H_2O (2 mL). The resulting mixture was cooled to 0 °C and 30% H_2O_2 (0.2 mL, 1.92 mmol) was added. Upon completion of

addition, the reaction mixture was allowed to warm to room temperature where it stirred for 16h. At the conclusion of this period, the reaction mixture was filtered and purified by preparative TLC using 5% chloroform in methanol to afford Example 6 (50 mg) as brown solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.74 (d, J = 1.8 Hz, 1H), 9.18-9.15 (dd, J = 11.2, 1.6 Hz, 2H), 8.34 (s, 1H), 8.24 (d, J = 4.4 Hz, 1H), 7.95-7.93 (dd, J = 8.4, 1.2 Hz, 1H), 7.88-7.84 (dt, J = 7.2, 1.6 Hz, 1H), 7.76-7.71 (dt, J = 8.0, 1.6 Hz, 2H), 7.59-7.52 (m, 5H), 7.37-7.31 (dd, J = 13.6, 8.0 Hz, 2H), 7.24 (t, J = 6.0 Hz, 1H), 6.94 (t, J = 4.0 Hz, 1H), 4.78 (d, J = 4.0 Hz, 2H). LCMS Method O: retention time 1.39 min; [M+1] = 433.0. HPLC Method B: purity 97.9%, retention time 8.06 min.

EXAMPLE 7

5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridine-3-sulfonamide



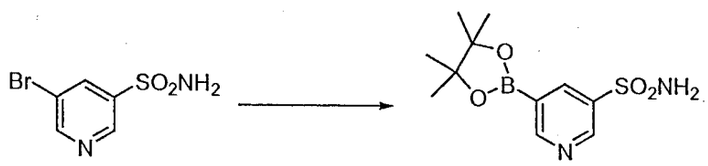
Step 1. Preparation of 5-Bromopyridine-3-sulfonamide



[00117] See also U.S. Publication Nos. 2006/217387 and 2006/375834, and *J. Org. Chem.*, 54:389 (1989). A mixture of pyridine-3-sulfonic acid (10.3 g, 64.8 mmol), phosphorous pentachloride (20.82 g, 100 mmol) and phosphorous oxychloride (10 mL, 109 mmol) was heated to reflux where it stirred for 4h. At the conclusion of this period, the reaction mixture was allowed to cool to room temperature. Once at the prescribed temperature, the reaction mixture was evaporated to dryness under reduced pressure to yield a residue. The residue was treated with bromine (6.00 mL, 116 mmol) and then heated to reflux where it stirred for 14h. After this time, the reaction mixture was cooled to 0 °C and then a saturated solution of NH_4OH in H_2O (40 mL)

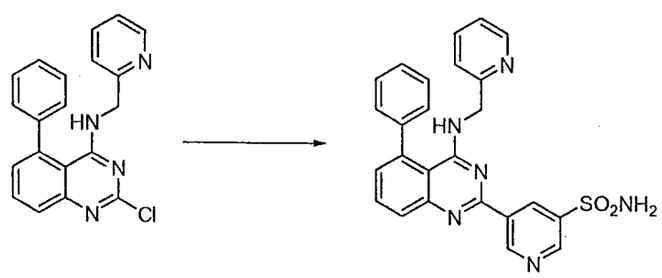
was slowly added. The resulting mixture was allowed to warm to room temperature where it stirred for 30 min. The reaction mixture was then filtered and the filter cake was washed with hexane to afford 5-bromopyridine-3-sulfonamide (6.0 g) as an off-white solid. The product was used without further purification. LCMS Method Q: retention time 0.75 min; [M+1] = 237.0.

Step 2. Preparation of pyridine-3-sulfonamide-5-ylboronic acid pinacol ester



[00118] See also WO2008/150827 A1 and WO2008/144463. A mixture of 5-bromopyridine-3-sulfonamide (1.5 g, 6.33 mmol), bis(pinacolato)diboron (2.41 g, 9.5 mmol) and potassium acetate (1.86 g, 19.0 mmol) in 1,4-dioxane (15 mL) was degassed with nitrogen for 15 min then (1,1'-bis(diphenylphosphino)-ferrocene)palladium (II) chloride dichloromethane complex (232 mg, 0.317 mmol) was added and the resulting mixture was degassed again with nitrogen for 10 min. At the conclusion of this period, the reaction mixture was heated in a microwave at 120 °C for 45 min. After this time, the reaction mixture was filtered through CELITE® and the filtrate was concentrated under reduced pressure to provide pyridine-3-sulfonamide-5-ylboronic acid pinacol ester (740 mg) as a brown solid. The product was used without further purification. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.83 (s, 1H), 8.80 (s, 1H), 8.26 (s, 1H), 7.56-7.74 (bs, 2H), 1.17 (s, 12H).

Step 3. Example 7

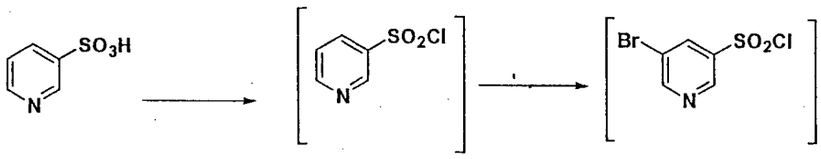


[00119] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (150 mg, 0.43 mmol) in 1,4-dioxane (6 mL) and H_2O (1 mL) under nitrogen

was added pyridine-3-sulfonamide-5-ylboronic acid pinacol ester (185 mg, 0.65 mmol), and potassium carbonate (119 mg, 0.86 mmol). Upon completion of addition, the mixture was degassed with nitrogen for 15 minutes and then (1,1'-bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (31 mg, 0.043 mmol) was added. The resulting mixture was again degassed with nitrogen for 10 min. After this time, the mixture was heated to 90 °C where it stirred for 16h. At the conclusion of this period, the reaction mixture was allowed to cool to room temperature. Once at the prescribed temperature, the reaction mixture was quenched by the addition of water and then transferred to a separation funnel. The aqueous layer was extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting concentrate was purified by preparative TLC using 5% methanol in dichloromethane to afford Example 7 (50 mg) as a brown solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.81 (s, 1H), 9.17 (s, 1H), 9.09 (s, 1H), 8.24 (d, J = 4.4 Hz, 1H), 7.94 (d, J =7.2 Hz, 1H), 7.86 (t, J = 7.6 Hz, 1H),7.75-7.72 (t, J = 7.6 Hz, 3H), 7.59-7.51 (m, 5H), 7.34 (d, J =7.2 Hz, 2H), 7.24 (t, J =6.4 Hz, 1H), 6.98 (t, J = 3.2 Hz, 1H), 4.77 (d, J = 4.0 Hz, 2H). LCMS Method Q: retention time 1.39 min; [M+1] = 469.0. HPLC Method B: purity 98.1%, retention time = 8.74 min.

[00120] Alternatively, Example 7 can be synthesized as follows:

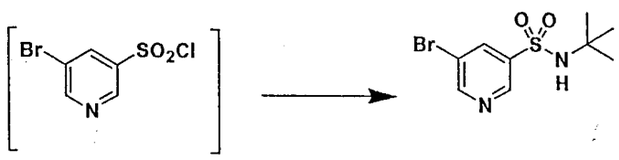
Step 1. Preparation of 5-Bromo-pyridine-3-sulfonyl chloride



[00121] PCl_5 (2.95 Kg, 14.16 moles) and $POCl_3$ (2.45 Kg, 15.98 moles) were added into pyridine-3-sulfonic acid (1.5 Kg, 9.42 mol) in 10 L RB flask equipped with mechanical stirrer under inert atmosphere. The reaction mass was heated to 120-125°C where it stirred for 18 h. After this time, the reaction progress was monitored

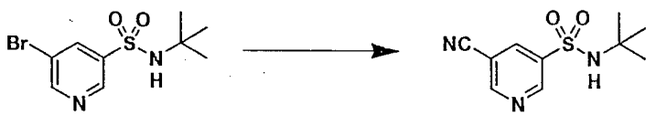
by HPLC, which indicated the reaction was complete. Excess $POCl_3$ was removed under vacuum to give a residue. The residue was cooled to ambient temperature and bromine (1.2 Kg, 7.5 moles) was added. Upon completion of addition, the resulting mixture was heated to 120-125°C where it stirred for 5 h. At the conclusion of this period, the reaction progress was monitored by HPLC, which indicated the reaction was complete. The reaction mixture was cooled to ambient temperature and then poured into ice-water (10 L), and the resulting mixture was extracted with DCM (10.5 L×2). The DCM extracts were combined and the solvent was removed under vacuum to yield crude product (1.8 Kg, 74.4% yield).

Step 2. Preparation of 5-bromo-N-tert-butylpyridine-3-sulfonamide



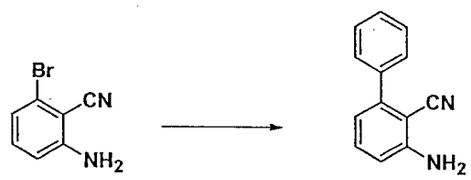
[00122] Crude 5-bromopyridine-3-sulfonyl chloride from step 1 above was dissolved in THF (14 L, 8 vol) and then transferred to a 20 L RB flask equipped with mechanical stirrer under inert atmosphere. The solution was cooled to 0-5°C and tert-butyl amine (1.95 Kg, 26.66 moles) was added at 0-5°C. Upon completion of addition, the reaction mixture was warmed to ambient temperature where it stirred for 2 h. At the conclusion of this period, the reaction progress was monitored by HPLC, which indicated that the reaction was complete. The solvent was evaporated under vacuum to give a thick residue. The residue was dissolved in ethyl acetate (18 L, 12 vol). The organic layer was separated, washed with water (9 L, 5 vol) and then concentrated under vacuum to yield a residue. Hexanes (9 L, 5 vol) were added to the residue and the product precipitated out and was collected by filtration to yield a free flowing yellow solid (1.5 Kg, 54.28% overall yield). ^{1}H NMR (DMSO-D6, 400 MHz, δ ppm); 8.99 (d, J = 2Hz, 1H), 8.81 (d, J = 2 Hz, 1H), 8.29 (t, J = 2Hz, 1H). $[M^+ + 1] = 293$.

Step 3. Preparation of 5-bromo-N-tert-butylpyridine-3-sulfonamide



[00123] 5-Bromo-N-tert-butylpyridine-3-sulfonamide (1.5 Kg, 5.11 moles) was dissolved in dimethylformamide (7.5 L, 5 vol) and the solution was added to a 20 L glass-lined reactor equipped with mechanical stirrer. The solution was degassed with nitrogen for 30 min. After this time, potassium ferrocyanide trihydrate (867 g, 2.05 moles), sodium carbonate (1.08 Kg, 10.189 moles), copper (I) iodide (73.2 g, 0.374 moles) and dichloro-bis (triphenylphosphine) palladium (II) (71.6 g, 0.102 moles) were added. Upon completion of addition, the reaction mixture was heated to 120-125°C where it stirred for 4 h. At the conclusion of this period, the reaction progress was monitored by HPLC, which indicated the reaction was complete. The reaction mixture was cooled to ambient temperature and then filtered through a celite bed. Water (18 L, 12 vol) was added into the filtrate and the resulting mixture was extracted with ethyl acetate (7.5L×2). The organic layers were combined, washed with water and then concentrated to yield a thick residue. Hexanes (7.5 L, 5 vol) were added to the residue. The product precipitated out and was collected by filtration to yield a free flowing yellow solid (1.0 Kg, 82.8% yield, 89% purity by HPLC). ^{1}H NMR (DMSO-D6, 400 MHz, δ ppm); 9.21 – 9.24 (d,d *J*= 7.2Hz, 3.2Hz, 2H), 8.70-8.71(m,1H), 7.98 (s,1H). [M^++1] = 239.2.

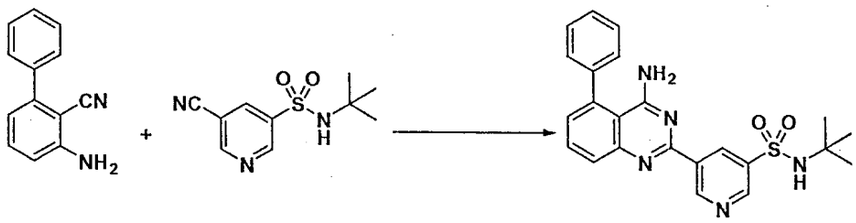
Step 4. Preparation of 3-aminobiphenyl-2-carbonitrile



[00124] 2-Amino-6-bromo-benzonitrile (1.0 Kg, 5.07 moles) and toluene (10 L, 10 vol) were added to a 20 L glass-lined reactor equipped with mechanical stirrer under inert atmosphere. Potassium acetate (996 g, 10.16 moles) and phenylboronic acid (866, 7.10 moles) were added into the solution and the solution was degassed with

nitrogen for 30 min. After this time, dichloro-bis (triphenylphosphine) palladium (II) (17.8 g, 0.025 moles) was added to the reaction mixture at ambient temperature. The mixture was heated to 110°C, where it stirred for 17 h. At the conclusion of this period, the reaction progress was monitored by HPLC, which indicated the reaction was completed. The reaction mixture was filtered through a celite bed. The filtrate was transferred back to the reactor and concentrated hydrochloric acid (~35%, 2 L, 2 vol) was charged to the reactor at ambient temperature. The HCl salt of the title compound precipitated out from the reaction and was collected by filtration. The HCl salt was transferred into the 20 L reactor and then made basic with 10% NaOH solution (pH 8-9). The resulting product was extracted with ethyl acetate (10 L, 10 vol). The ethyl acetate layer was washed with water (5 L, 5 vol) and then the solvent was evaporated under vacuum to give a residue. Hexanes (5 L, 5 vol) were added to the residue at 35-40°C, and the resulting slurry was cooled to ambient temperature. Once at the prescribed temperature, the product was collected by filtration to provide a pale yellow solid (802 g, 81.4%, 99% by HPLC). ^{1}H NMR (DMSO-D6, 400 MHz, δ ppm); 7.43-7.52 (m, 5H), 7.33-7.37 (m, 1H), 6.83 (d, *J*=8Hz, 1H), 6.62 (d, *J*=8Hz, 1H), 6.1 (s, 2H). ES-MS: [M^++1] = 194.23.

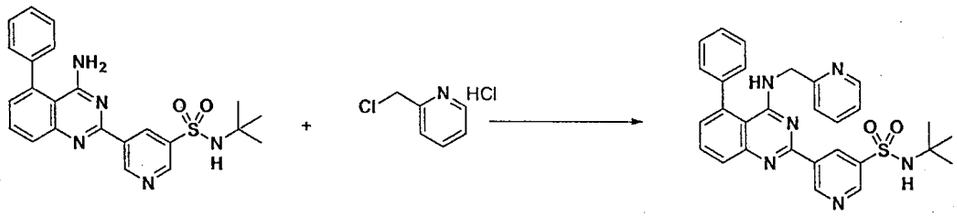
Step 5. Preparation of 5-(4-amino-5-phenylquinazolin-2-yl)-N-tert-butylpyridine-3-sulfonamide



[00125] 3-Aminobiphenyl-2-carbonitrile (1028 g, 5.30 moles), 5-bromo-N-tert-butylpyridine-3-sulfonamide (1440 g, 5.55 moles) and 1,4-dioxane (10 L, 10 vol) were added to a 20 L glass-lined reactor equipped with mechanical stirrer. Sodium tert-butoxide (1.275 Kg 12.870 moles) was added to the solution portion-wise at 20-30°C. Upon completion of addition, the reaction mixture was heated to reflux where it stirred for 2 h. At the conclusion of this period, the reaction progress was monitored by HPLC, which indicated the reaction was complete. The reaction

mixture was cooled to 30-35°C and then poured into water (40 L, 40 vol). The resulting mixture was extracted with DCM (20 L×2). The DCM layers were combined, washed with water (10 L, 10 vol) and then dried over sodium sulfate. The solvent was evaporated under vacuum to give a residue. Isopropyl alcohol (1.2 L, 1.2 vol) was added to the residue at 40°C. The resulting precipitate slurry was cooled to 10-15°C and then stirred for 2 h. After this time, the precipitate was collected by filtration and dried at 50°C for 16 h to yield the product (1.9 Kg, 82.9% yield, 99% purity by HPLC). ^{1}H NMR (DMSO-D6, 400 MHz, δ ppm); 9.72 (s, 1H), 9.11 (s, 2H), 7.83-7.94 (m, 4H), 7.49-7.60 (m, 5H), 7.31 (d,d *J*=6.8Hz,1.2Hz, 1H). ES-MS: [M^++1] = 433.53.

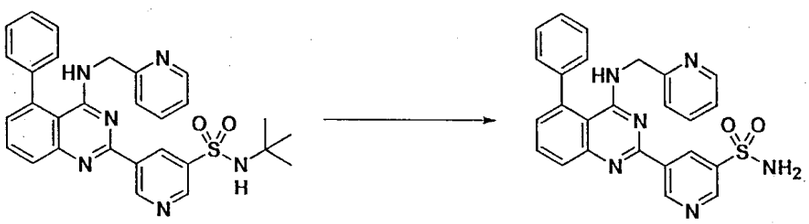
Step 6. Preparation of N-tert-butyl-5-(5-phenyl-4-(pyridin-2-ylmethylamino) quinazolin-2-yl) pyridine-3-sulfonamide



[00126] 2-(Chloromethyl) pyridine hydrochloride (564 g, 3.44 moles) and dimethyl acetamide (7L, 7 vol) were added to a 20 L RB flask-1 equipped with mechanical stirrer under inert atmosphere. The resulting solution was cooled to 0-5°C and triethylamine (346.3, 3.44 moles) was added at 0-5°C. 5-(4-Amino-5-phenylquinazolin-2-yl)-N-tert-butylpyridine-3-sulfonamide (1.0 Kg. 2.306 moles) and dimethylacetamide (4 L, 4 vol) were added to a separate 20 L RB flask-2 equipped with mechanical stirrer under inert atmosphere. This solution was cooled to 0-5°C and sodium tert-butoxide (884 g, 9.24 moles) was added at 0-5°C. The resulting solution was stirred to affect dissolution and then transferred to the RB flask-1 at 0-5°C. Upon completion of addition, the reaction mixture was stirred at 0-5°C for 2 h. At the conclusion of this period, the reaction progress was monitored by HPLC, which indicated that the reaction was complete. The reaction mass was poured into water (60 L, 60 vol) with stirring. The crude product was collected by filtration and dried at 60°C for 12 h. After this time, the dried material was dissolved in THF (20

L, 20 vol). Upon dissolution, 6M HCl in isopropyl alcohol (1 L, 1 vol) was added at 20-25°C. The crude HCL salt of the product was obtained a pale-yellow free flow solid (920 g, 71% yield, 93% purity by HPLC). The crude HCl salt (1.345 Kg, 2.56moles), methanol (6.7 L, 5 vol) and dichloromethane (13.5 L, 10 vol) were added to a 20 L glass-lined reactor equipped with mechanical stirrer. The slurry was stirred for 20-30 min at 30°C. After this time, the solvent was distilled to 4 vol with respect to input under vacuum. The resulting slurry was cooled to 20-25°C, where stirred for 2 h. At the conclusion of this period, the slurry was filtered and dried at 50°C for 6 h to yield the product (1.1 Kg, 82% yield, 98% purity by HPLC). ^{1}H NMR (DMSO-D6, 400 MHz, δ ppm); 9.72 (s, 1H), 9.10-9.14 (m, 2H), 8.39 (s, 1H), 7.92-8.03 (m, 4H), 7.56-7.58 (m, 5H), 7.43-7.49 (m, 3H), 7.1 (bs, 1H), 4.88 (s, 2H), 1.17 (2, 9H).

Step 7. Example 7

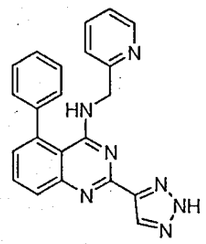


[00127] N-tert-butyl-5-(5-phenyl-4-(pyridin-2-ylmethylamino) quinazolin-2-yl) pyridine-3-sulfonamide (1.0 Kg, 1.9 moles) and concentrated hydrochloric acid (7 L, 7 vol) were added to a 20 L glass-lined reactor equipped with mechanical stirrer. The reaction mixture was heated to 90-100°C where it stirred for 1 h. At the conclusion of this period, the reaction progress was monitored by HPLC, which indicated the reaction was complete. The reaction mixture was cooled to 5-10°C and the pH was adjusted to 1.7 to 2.0 using 12% aqueous sodium hydroxide solution. Once at the prescribed pH, the crude HCl salt of the product was collected by filtration. The HCl salt filter cake and ethanol (5 L, 5 vol) were added to 10 L glass-lined reactor equipped with a mechanical stirrer. The resulting mixture was made basic to pH 7-8 at 20-25°C using triethyl amine (2.25 Kg, 22.23 moles). Once at the prescribed pH, the basic mixture was stirred for 2 h. After this time, the free base of product was filtered and washed with water (10 L, 10 vol) followed by ethanol (2L, 2 vol). The resulting product was dried at 50-55°C for 8 h to yield Example 7 (644 g, 72% yield,

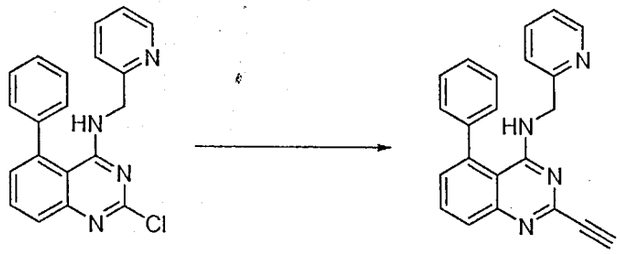
99.9% purity by HPLC). ^{1}H NMR (DMSO-D6, 400 MHz, δ ppm); 9.81 (d, *J*=2.0Hz, 1H), 9.18 (t, J=2Hz, 1H), 9.11 (d, J=2Hz, 1H), 8.23 (d, J=4.4Hz, 1H), 7.92-7.94 (m, 1H), 7.83-7.87 (m, 1H), 7.78 (s, 2H), 7.70-7.72 (m, 1H), 7.50-7.59 (m, 5H), 7.31-7.34 (m, 2H), 7.22-7.25 (m, 1H), 6.95 (t, J=4Hz, 1H), 4.76 (d, *J*=4Hz, 2H). ES-MS: $[M^+ +1] = 469$.

EXAMPLE 8

5-Phenyl-N-(pyridin-2-ylmethyl)-2-(2H-1,2,3-triazol-4-yl)quinazolin-4-amine



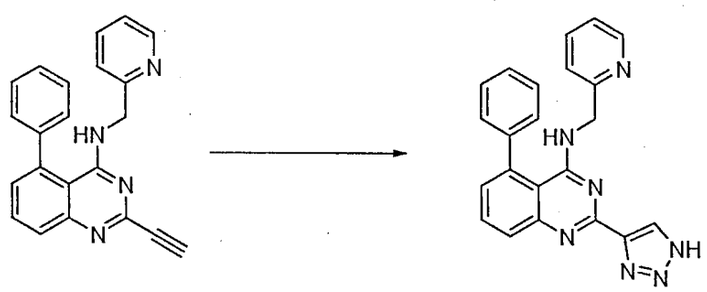
Step 1. Preparation of 2-ethynyl-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine



[00128] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (1.0 g, 2.8 mmol) in DMF (10 mL) under nitrogen was added trimethylsilylacetylene (2.0 mL, 14 mmol), cupric iodide (0.11g, 0.58mmol) and Et_3N (1.2 mL, 8.4mmol). Upon completion of addition, the mixture was degassed with nitrogen for 15 min. Tetrakis(triphenylphosphine)palladium (0.20 g, 0.28mmol) was then added and the resulting mixture was again degassed with nitrogen for 10 min. After this time, the reaction mixture was heated in a sealed tube to 120 °C where it stirred for 16h. At the conclusion of this period, the reaction mixture was allowed to cool to room temperature. Once at the prescribed temperature, the reaction mixture was quenched by the addition of water. The resulting reaction mixture was extracted with ethyl acetate and the organic layer was washed successively with water and

brine. The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting concentrate was dissolved in methanol and saturated with ammonia gas. The saturated solution was stirred for 2h at 0 °C and then concentrated under reduced pressure to yield a residue. The residue was purified by flash column chromatography using ethyl acetate and petroleum ether to afford 2-ethynyl-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (650 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.15 (d, J = 4.0 Hz, 1H), 7.86 (dd, J = 8.4, 1.2 Hz, 1H), 7.69 (t, J = 8.4 Hz, 1H), 7.56 (dt, J = 3.6, 1.6 Hz, 1H), 7.49-7.42 (m, 5H), 7.26-7.23 (m, 1H), 7.13-7.08 (m, 2H), 6.94 (bs, 1H), 4.67 (d, J = 10.0 Hz, 2H), 3.02 (s, 1H). LCMS Method O: retention time 1.35 min, [M+1] = 337.0.

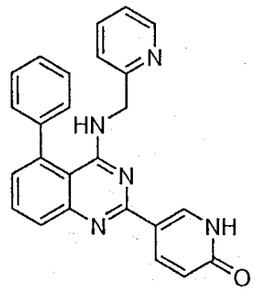
Step 2. Example 8



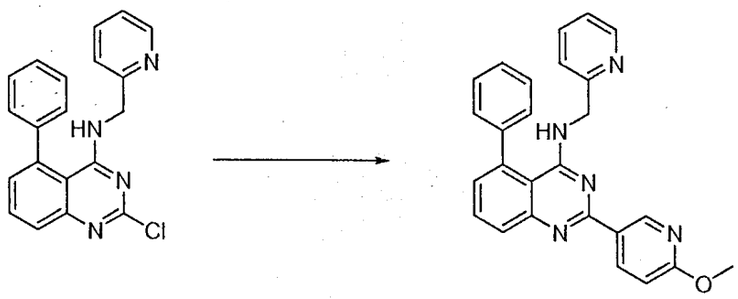
[00129] To a suspension of 2-ethynyl-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.17g, 0.50 mmol) in toluene (3 mL) was added trimethylsilylazide (0.20 ml, 1.5 mmol). Upon completion of addition, the reaction mixture was heated in sealed tube to 120 °C where it was maintained for 2days. At the conclusion of this period, the toluene was removed under reduced pressure to yield a residue. The residue was washed with water and then extracted with dichloromethane. The organic extracts were dried over Na_2SO_4, filtered and then concentrated. The resulting concentrate was purified by flash column chromatography on silica gel eluting with chloroform and methanol (ratio 95:5) to afford Example 8 (90 mg) as a yellow solid. ^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 8.42 (bs, 1H), 8.33 (d, J = 10.0 Hz, 1H), 7.92 (d, J = 10.0 Hz, 1H), 7.83 (t, J = 11.2 Hz, 1H), 7.76-7.72 (m, 2H), 7.49 (m, 5H), 7.31 (d, J = 10.8 Hz, 1H), 7.30-7.25 (m, 2H), 4.78 (s, 2H). LCMS Method O: retention time 1.36 min, [M+1] = 380.2. HPLC Method B: purity 98.5%, retention time 10.03 min.

EXAMPLE 10

5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-2(1H)-one



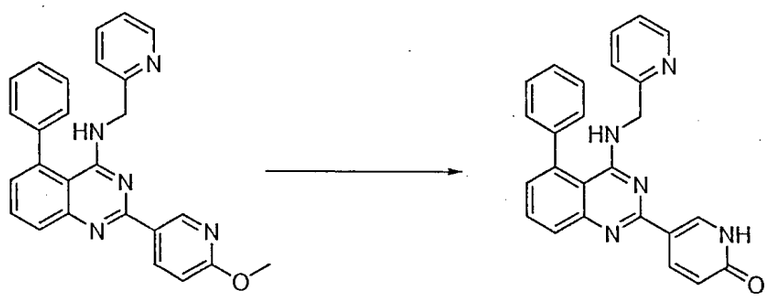
Step 1. Preparation of 2-(6-methoxypyridin-3-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine



[00130] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (200 mg, 0.58 mmol) in DMF (10 mL) and H_2O (2 mL) under nitrogen was added 6-methoxypyridin-3-ylboronic acid pinacol ester (202 mg, 0.86 mmol) and potassium carbonate (160 mg, 1.16 mmol). Upon completion of addition, the mixture was degassed with nitrogen for 15 min and then tetrakis(triphenylphosphine)-palladium (66 mg, 0.0050 mmol) was added. The mixture was again degassed with nitrogen for 10 min. After this time, the reaction mixture was heated to 90 °C where it stirred for 12h. The reaction mixture was then allowed to cool to room temperature and then quenched by the addition of water. The reaction mixture was extracted with ethyl acetate and the organic layer was washed successively with water and brine. The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting concentrate was purified by flash column chromatography using 16% ethyl acetate in petroleum ether to afford 2-(6-methoxypyridin-3-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (140 mg)

as a brown solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.26 (d, J = 2.4 Hz, 1H), 8.70-8.67 (dd, J = 8.8, 2.4 Hz, 1H), 8.23-8.22 (d, J = 5.2 Hz, 1H), 7.84-7.76 (m, 2H), 7.73-7.69 (dt, J = 8.0, 2.0 Hz, 1H), 7.58-7.48 (m, 5H), 7.32-7.30 (d, J = 7.6 Hz, 1H), 7.25-7.23 (m, 2H), 6.95-6.93 (d, J = 8.8 Hz, 1H), 6.81-6.79 (t, J = 4.0 Hz, 1H), 4.72-4.71 (d, J = 4.0 Hz, 2H), 3.94 (s, 3H). LCMS Method S: retention time 3.96 min, [M+1] = 420.2. HPLC Method B: purity 98.9%, retention time 8.93 min.

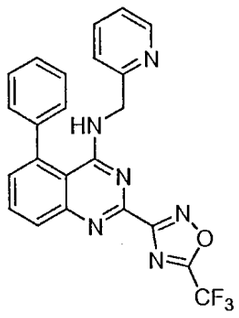
Step 2. Example 10



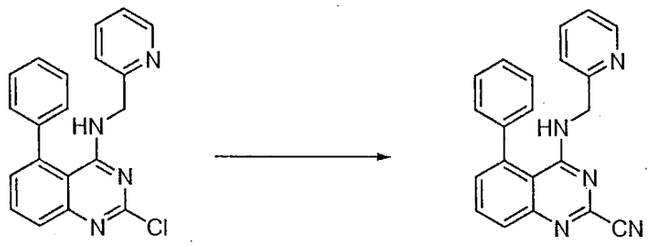
[00131] To a solution of 2-(6-methoxypyridin-3-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (140 mg, 0.33 mmol) in CH_2Cl_2 (2 mL) was slowly added BBr_3 (416 mg, 1.66 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 72h before it was quenched by the addition of aqueous solution of ammonium hydroxide. The reaction mixture was then extracted with CH_2Cl_2. The organic layer was washed successively with water and brine. The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting concentrate was purified by preparative HPLC to afford Example 10 (75 mg) as an off-white solid. Preparative HPLC Conditions: Column: Sunfire C18 (250 x 19 mm), Mobile Phase A: 0.1% TFA in H_2O, Mobile Phase B: CH_3CN, Gradient: 0 to 40% B over 25 min, 100% B for 10 min., Flow Rate: 14 mL/min., Retention time: 20.5 min. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm):8.68 (s, 1H), 8.41-8.38 (dd, J = 9.6, 2.8 Hz, 1H), 8.23 (d, J = 4.4 Hz, 1H), 8.09-7.94 (m, 3H), 7.84-7.79 (dt, J = 7.6, 1.6 Hz, 1H), 7.65-7.54 (m, 5H), 7.50-7.48 (d, J = 7.2 Hz, 1H), 7.40-7.38 (d, J = 8.0 HZ, 1H), 7.33-7.30 (t, J = 6.8 Hz, 1H), 6.62-6.60 (d, J = 9.6 Hz, 1H), 4.88 (d, J = 4.0 Hz, 2H). LCMS Method O: retention time 1.35 min, [M+1] = 406.2. HPLC Method B: purity 99.2%, retention time 10.26min.

EXAMPLE 11

5-Phenyl-N-(pyridin-2-ylmethyl)-2-(5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl)quinazolin-4-amine

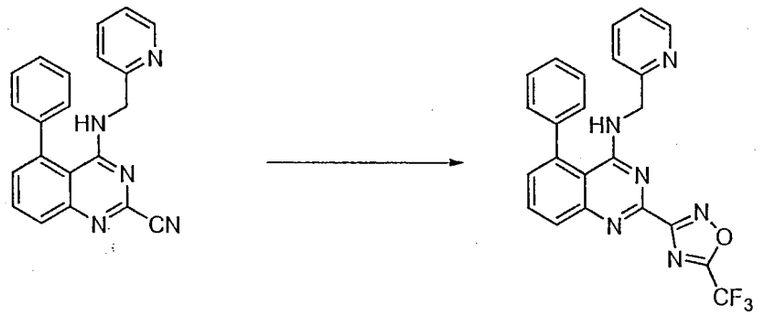


Step 1. Preparation of 5-Phenyl-4-(pyridin-2-ylmethylamino)quinazoline-2-carbonitrile



[00132] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (5.0 g, 14 mmol) in CH_3CN (50 mL) was added tetramethylammonium cyanide (4.5 g, 29 mmol) followed by DBU (4.39 g, 28.88 mmol). Upon completion of addition, the reaction mixture was heated to 80 °C where it stirred for 12h. After this time, the reaction mixture was quenched with water and then extracted with ethyl acetate. The organic layer was washed successively with water and brine, and the combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting concentrate was purified by flash column chromatography using 28% ethyl acetate in petroleum ether to yield 5-phenyl-4-(pyridin-2-ylmethylamino)quinazoline-2-carbonitrile (2.1 g) as a brown solid. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.15-8.14 (d, J = 4.0 Hz, 1H), 7.96-7.87 (m, 2H), 7.75-7.70 (dt, J = 7.6, 2.0 Hz, 1H), 7.62-7.45 (m, 6H), 7.34-7.29 (m, 2H), 7.25-7.22 (m, 1H), 4.60 (d, J = 3.6 Hz, 2H). LCMS Method O: retention time 1.52 min, [M+1] = 338.2.

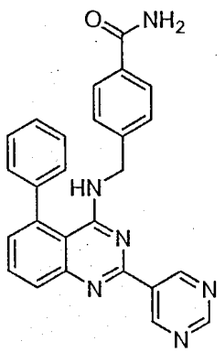
Step 2. Example 11



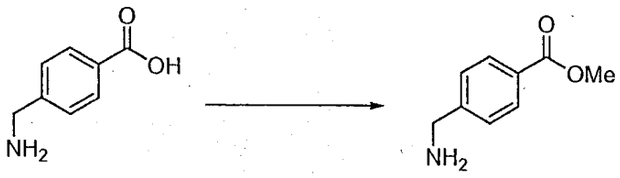
[00133] To a solution of 5-phenyl-4-(pyridin-2-ylmethylamino)quinazoline-2-carbonitrile (150 mg, 0.45 mmol) in EtOH (5 mL) was added NH_2OH-HCl (62 mg, 0.90 mmol) followed by Et_3N (125 μL, 0.90 mmol). The reaction mixture was heated to reflux where it stirred for 4h. After this time, the reaction mixture was concentrated under reduced pressure to yield a residue. The residue was dissolved in THF (5 mL). The resulting solution was cooled to 0 °C and pyridine (145 μL, 1.80 mmol) followed by trifluoroacetic anhydride (125 μL, 0.90 mmol) were added. Upon completion of addition, the reaction mixture was warmed to room temperature where it stirred for 16h. At the conclusion of this period, the reaction mixture was concentrated under reduced pressure to yield a residue. The residue was purified by flash column chromatography using 36% ethyl acetate in petroleum ether to afford Example 11 (65 mg) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.19 (d, J = 4.0 Hz, 1H), 7.99-7.91 (m, 2H), 7.75-7.71 (t, J = 7.2 Hz, 1H), 7.60-7.54 (m, 5H), 7.44 (d, J = 6.4 Hz, 1H), 7.36 (d, J = 7.6 Hz, 1H), 7.26-7.23 (m, 1H), 7.19 (m, 1H), 4.68-4.67 (d, J = 3.6 Hz, 1H). LCMS Method O: retention time 1.71 min, [M+1] = 449.0. HPLC Method B: purity 99.5%, retention time 9.66 min.

EXAMPLE 12

4-((5-Phenyl-2-(pyrimidin-5-yl)quinazolin-4-ylamino)methyl)benzamide

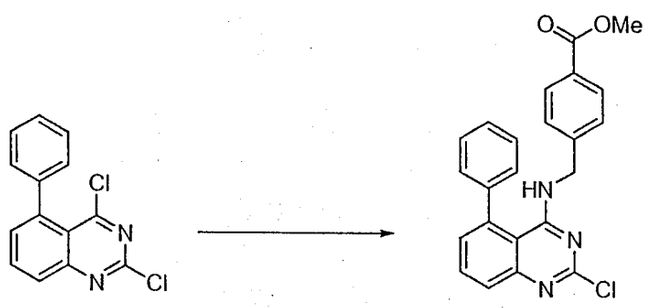


Step 1. Preparation of methyl 4-(aminomethyl)benzoate



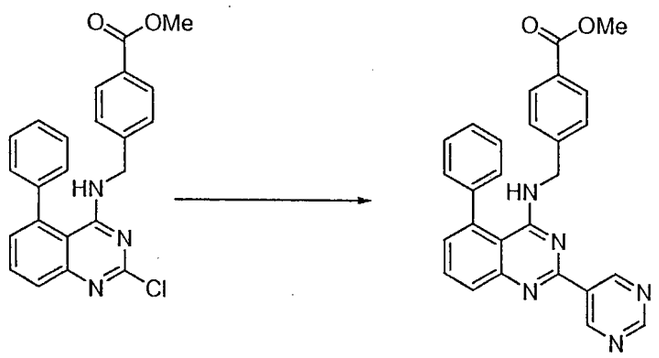
[00134] To a solution of 4-(aminomethyl)benzoic acid (1 g, 7 mmol) in MeOH (10 mL) was added dropwise concentrated H_2SO_4 (1 mL). Upon completion of addition, the reaction mixture was heated to 60 °C where it stirred for 12h. After this time, the reaction mixture was concentrated under reduced pressure to yield a residue. The residue was dissolved in ethyl acetate and then carefully neutralized with a 10% NaOH solution. The organic layer was separated and washed successively with water and brine. The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford methyl 4-(aminomethyl)benzoate (2.5 g) as a white solid. LCMS Method O: retention time 0.49 min, [M+1] = 166.2.

Step 2. Preparation of methyl 4-((2-chloro-5-phenylquinazolin-4-ylamino)-methyl)benzoate



[00135] To a solution of 2,4-dichloro-5-phenylquinazoline (1 g, 4 mmol) in THF (15 mL) was added diisopropylethyl amine (1.86 mL, 10.9 mmol) followed by methyl 4-(aminomethyl)benzoate (1.19 g, 7.21 mmol). Upon completion of addition, the reaction mixture was stirred for 12h. At the conclusion of this period, the reaction mixture was diluted with ethyl acetate and then washed successively with water and brine. The combined organic layers were dried over Na_2SO_4, filtered and concentrated to yield a residue. The residue was purified by flash column chromatography using 6% ethyl acetate in petroleum ether to afford methyl 4-((2-chloro-5-phenylquinazolin-4-ylamino)methyl)benzoate (600 mg) as a white solid. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.92 (d, J = 8.0 Hz, 2H), 7.80 (d, J = 8.4 Hz, 1H), 7.70 (t, J = 8.0 Hz, 1H), 7.38-7.33 (m, 5H), 7.22 (d, J = 7.2 Hz, 1H), 7.02 (d, J = 8.0 Hz, 2H), 5.56 (bs, 1H), 4.53 (d, J = 4.8 Hz, 2H), 3.39 (s, 3H). LCMS Method O: retention time 2.12 min, [M+1] = 404.0. HPLC Method B: purity 97.8%, retention time 18.17 min.

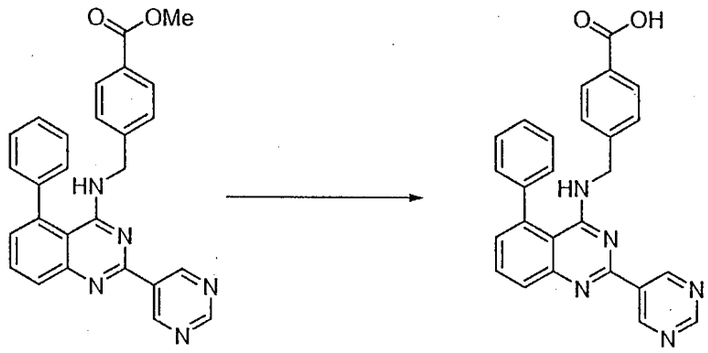
Step 3. Preparation of methyl 4-((5-phenyl-2-(pyrimidin-5-yl)quinazolin-4-ylamino)methyl)benzoate



[00136] To a solution of methyl 4-((2-chloro-5-phenylquinazolin-4-ylamino)methyl)benzoate (550 mg, 1.36 mmol) in DMF (16 mL) and H_2O (0.5 mL) under nitrogen were added pyrimidine-5-ylboronic acid pinacol ester (422 mg, 2.04 mmol) and potassium carbonate (377 mg, 2.72 mmol). The resulting mixture was degassed with nitrogen for 15 min and then (1,1'-bis(diphenylphosphino)ferrocene)-palladium (II) chloride dichloromethane complex (50 mg, 0.068 mmol) was added. Upon completion of addition, the reaction mixture was again degassed for 10 min. with nitrogen. The reaction mixture was then heated to 110 °C where it stirred for

12h. After this time, the reaction mixture was allowed to cool to room temperature. Once at the prescribed temperature, the reaction mixture was quenched by the addition of water and then extracted with ethyl acetate. The organic layer was washed successively with water and brine. The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting concentrate was purified by flash column chromatography using 0.5% MeOH in CH_2Cl_2 to afford methyl 4-((5-phenyl-2-(pyrimidin-5-yl)quinazolin-4-ylamino)methyl)benzoate (400 mg) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.62 (s, 2H), 9.31 (s, 1H), 7.93-7.86 (m, 4H), 7.54-7.49 (m, 5H), 7.37 (d, J = 6.8 Hz, 1H), 7.28 (d, J = 8.0 Hz, 2H), 5.94 (t, J = 4.8 Hz, 1H), 4.71 (d, J = 5.2 Hz, 1H), 3.85 (s, 3H). LCMS Method C: retention time 2.15 min, [M+1] = 448.2. HPLC Method B: purity 98.5%, retention time 9.81 min.

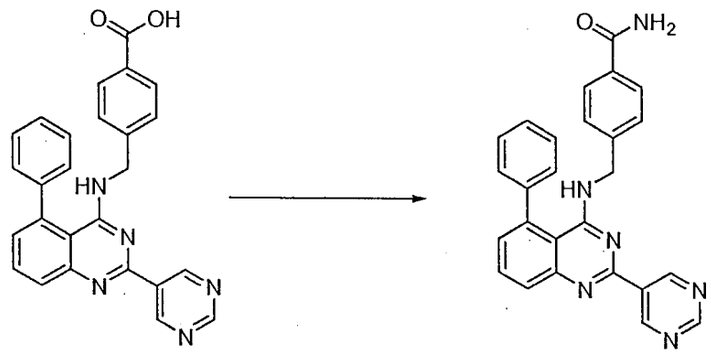
Step 4. Preparation of 4-((5-phenyl-2-(pyrimidin-5-yl)quinazolin-4-ylamino)methyl)benzoic acid



[00137] To a solution of methyl 4-((5-phenyl-2-(pyrimidin-5-yl)quinazolin-4-ylamino)methyl)benzoate (400 mg, 0.89 mmol) in MeOH-THF-H_2O (6 mL-6 mL-0.5 mL) was added LiOH (112 mg, 2.67 mmol). Upon completion of addition, the reaction mixture was heated to 45 °C where it stirred for 12h. After this time, the reaction mixture was concentrated under reduced pressure to remove the MeOH and THF and then carefully acidified with 1.5N HCl. The resulting precipitate was collected by filtration to afford 4-((5-phenyl-2-(pyrimidin-5-yl)quinazolin-4-ylamino)methyl)benzoic acid (250 mg) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.87 (bs, 1H), 9.68 (s, 2H), 9.39 (s, 1H), 8.09 (m, 1H), 7.98 (t, J = 8.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 2H), 7.53-7.48 (m, 6H), 7.26 (d, J = 8.0 Hz, 2H),

6.65 (bs, 1H), 4.78 (d, J = 5.2 Hz, 2H). LCMS Method O: retention time 1.73 min, [M+1] = 434.2. HPLC Method B: purity 98.1%, retention time 8.24 min.

Step 5. Example 12



[00138] To a solution of 4-((5-phenyl-2-(pyrimidin-5-yl)quinazolin-4-ylamino)methyl)benzoic acid (75 mg, 0.17 mmol), EDC-HCl (40 mg, 0.21 mmol), and HOBt (28 mg, 0.21 mmol) in DMF (4 mL) was added diisopropylethyl amine (120 μL, 0.69 mmol) followed by NH_4Cl (37 mg, 0.69 mmol). Upon completion of addition, the reaction mixture was stirred at room temperature for 12h, and then diluted with ethyl acetate. The organic layer was washed successively with water and brine. The organic portion was separated, dried over Na_2SO_4, filtered and then concentrated under reduced pressure. The resulting concentrate was purified by flash column chromatography using 3% MeOH in CH_2Cl_2 to afford Example 12 (25 mg) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.65 (s, 2H), 9.31 (s, 1H), 7.94-7.85 (m, 3H), 7.79 (d, J = 8.0 Hz, 2H), 7.52-7.49 (m, 5H), 7.36 (m, 2H), 7.17 (d, J = 8.0 Hz, 2H), 5.89 (t, J = 4.8 Hz, 1H), 4.66 (d, J = 4.8 Hz, 2H). LCMS Method O: retention time 1.49 min, [M+1] = 433.2. HPLC Method B: purity 98.4%, retention time 7.52 min.

EXAMPLE 16

2-Chloro-5-phenyl-N-(pyridin-2-yl)quinazolin-4-amine



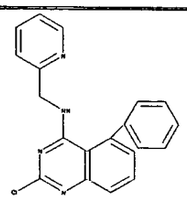
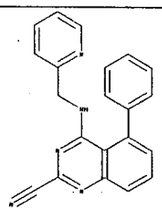
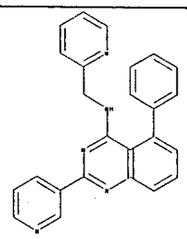
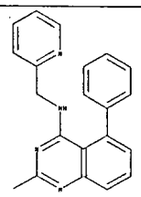
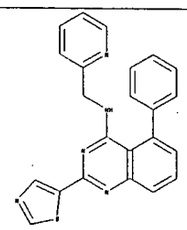
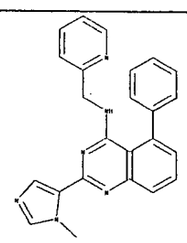
[00139] To a suspension of NaH (13 mg, 0.547 mmol) in THF (2 mL) at 0 °C was added a solution of 3-aminopyridine (26 mg, 0.273 mmol) in THF (2 mL). Upon completion of addition, the reaction mixture was stirred at 0 °C for 30 min. At the conclusion of this period, a solution of 2,4-dichloro-5-phenylquinazoline (75 mg, 0.273 mmol) in THF (2 mL) was added. The reaction mixture was allowed to warm to room temperature where it stirred for 16h. After this time, the reaction mixture was quenched with a saturated aqueous solution of NH_4Cl, and the resulting solution was extracted with ethyl acetate. The organic layer was washed successively with water and brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting concentrate was purified by flash column chromatography using 30% ethyl acetate in petroleum ether to afford Example 16 (15 mg) as a white solid. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.53-8.51 (d, J = 8.4 Hz, 1H), 8.11-8.09 (dd, J = 4.0, 1.2 Hz, 1H), 7.92-7.88 (m, 2H), 7.82-7.78 (t, J = 7.6 Hz, 1H), 7.73-7.69 (dt, J = 8.0, 1.6 Hz, 1H), 7.62-7.60 (m, 3H), 7.52-7.50 (m, 2H), 7.39-7.37 (d, J = 7.2 Hz, 1H), 6.97-6.94 (dd, J = 7.2, 4.8 Hz, 1H). LCMS Method M: retention time 1.73 min, [M+1] = 333.2. HPLC Method B: purity 99.7%, retention time 17.30 min.

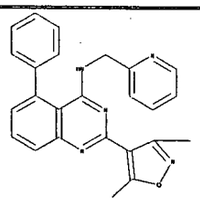
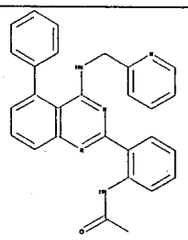
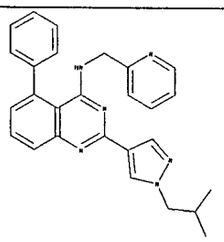
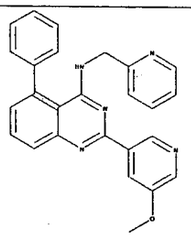
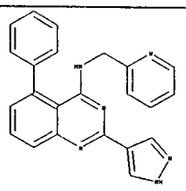
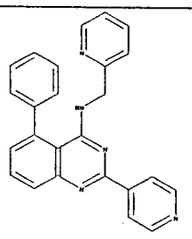
EXAMPLES 19 through 58

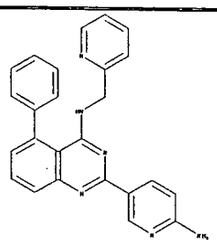
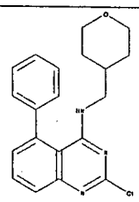
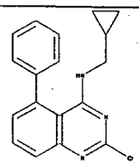
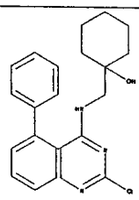
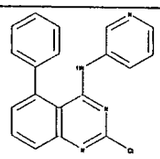
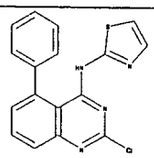
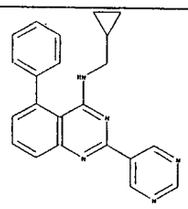
[00140] Examples 19 through 58 were synthesized via similar procedures described above. HPLC/MS data for each compound was collected using method E, and the molecular mass determined by MS (ES) by the formula m/z. Both the retention time and MS data for the examples are listed in Table 1a, wherein MW = molecular weight.

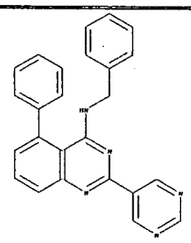
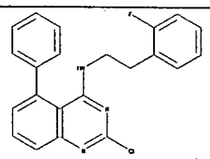
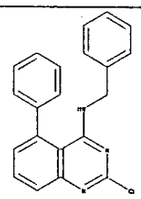
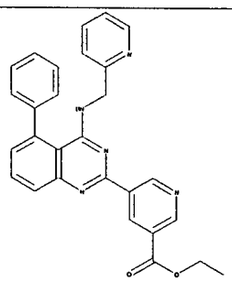
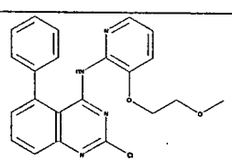
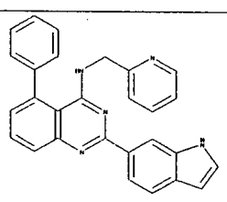
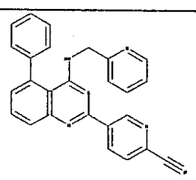
TABLE 1a

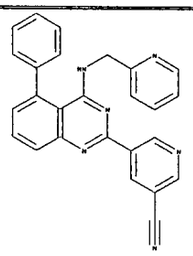
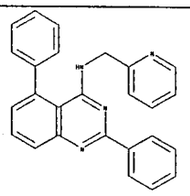
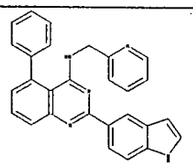
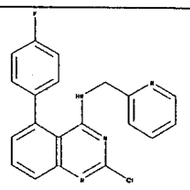
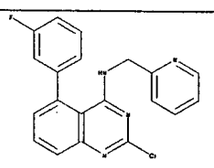
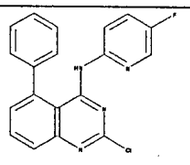
Example	Structure	MW	LCMS Data	LCMS Method

Example	Structure	MW	LCMS Data	LCMS Method
19		346.813	[M+1] 347.0 Rt: 0.95 min	A
20		337.377	[M+1] 338.3 Rt: 0.88 min	D
21		389.452	[M+1] 390.3 Rt: 0.73 min	D
22		326.394	[M+1] 327.1 Rt: 0.65 min	A
23		395.48	[M+1] 396.3 Rt: 0.86 min	D
24		392.456	[M+1] 393.2 Rt: 0.72 min	A

Example	Structure	MW	LCMS Data	LCMS Method
25		407.467	[M+1] 408.2 Rt: 1.525 min	M
26		445.515	[M+1] 446.2 Rt: 1.477 min	M
27		434.536	[M+1] 435.2 Rt: 1.667 min	M
29		419.478	[M+1] 420.2 Rt: 1.631 min	N
30		378.429	[M+1] 379.2 Rt: 1.359 min	M
31		389.452	[M+1] 390.2 Rt: 1.370 min	M

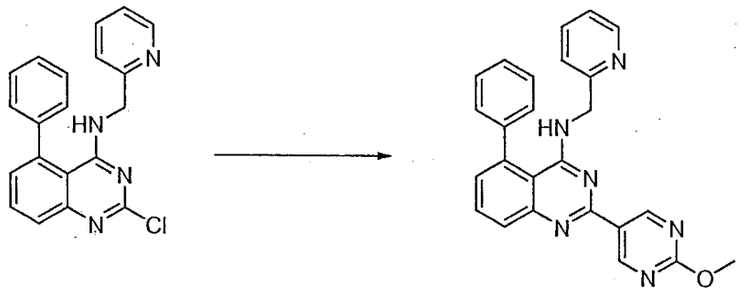
Example	Structure	MW	LCMS Data	LCMS Method
32		404.467	[M+1] 405.2 Rt: 1.298 min	M
34		353.845	[M+1] 354.2 Rt: 1.675 min	O
35		309.793	[M+1] 310.2 Rt: 1.893 min	O
36		367.872	[M+1] 368.2 Rt: 1.857 min	O
37		332.786	[M+1] 333.2 Rt: 1.888 min	N
38		338.814	[M+1] 339.0 Rt: 1.907 min	O
39		353.42	[M+1] 354.2 Rt: 1.626 min	O

Example	Structure	MW	LCMS Data	LCMS Method
40		389.452	[M+1] 390.2 Rt: 1.810 min	O
41		377.842	[M+1] 378.2 Rt: 2.042 min	O
42		345.825	[M+1] 346.2 Rt: 2.000 min	O
43		461.515	[M+1] 462.2 Rt: 2.138 min	Q
45		406.865	[M+1] 407.2 Rt: 1.656 min	Q
46		427.5	[M+1] 428.2 Rt: 1.622 min	O
47		414.461	[M+1] 415.2 Rt: 2.036 min	M

Example	Structure	MW	LCMS Data	LCMS Method
48		414.461	[M+1] 415.2 Rt: 1.653 min	O
50		388.464	[M+1] 389.2 Rt: 1.605 min	O
51		427.5	[M+1] 428.2 Rt: 1.663 min	O
54		364.803	[M+1] 365.2 Rt: 1.517 min	O
55		364.803	[M+1] 365.2 Rt: 1.530 min	O
58		350.777	[M-1] 349.0 Rt: 3.084 min	P

EXAMPLE 62

2-(2-methoxypyrimidin-5-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine



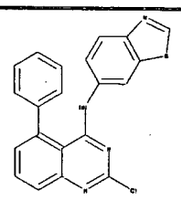
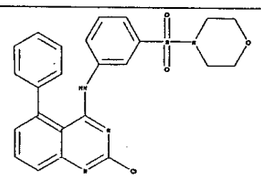
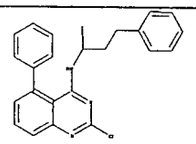
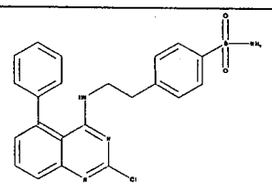
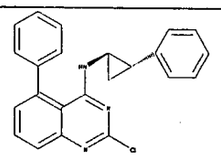
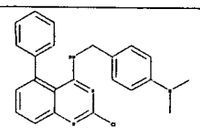
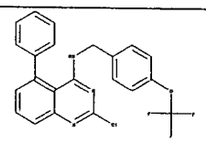
[00141] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (300 mg, 0.87 mmol) in DMF (20 mL) and H_2O (2 mL) under nitrogen was added 2-methoxypyrimidin-5-ylboronic acid (199 mg, 1.30 mmol) and potassium carbonate (239 mg, 1.73 mmol). The resulting mixture was degassed with nitrogen for 15 min and then tetrakis(triphenylphosphine)palladium (100 mg, 0.086 mmol) was added. Upon completion of addition, the reaction mixture was again degassed with nitrogen for 10 min. After this time, the reaction mixture was heated to 90 °C where it stirred for 12h. After this time, the reaction mixture was allowed to cool to room temperature and then quenched by the addition of water. The reaction mixture was extracted with ethyl acetate and the organic layer was washed successively with water and brine. The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting concentrate was purified by preparative HPLC to afford 2-(2-methoxypyrimidin-5-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (205 mg) as an off-white solid. Preparative HPLC Conditions: Column: Sunfire C18 (250 x 19 mm), Mobile Phase A: 0.1% TFA in H_2O, Mobile Phase B: CH_3CN, Gradient: 0 to 40% B over 35 min, 100% B for 10 min., Flow Rate: 14 mL/min., Retention time: 28 min. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.50 (s, 2H), 8.27 (d, J = 4.7 Hz, 1H), 7.92 (d, J = 3.6 Hz, 2H), 7.85-7.81 (t, J = 8.0 Hz, 1H), 7.60-7.52 (m, 5H), 7.42-7.38 (m, 2H), 7.34-7.31 (m, 1H), 4.83 (d, J = 4.2 Hz, 2H), 4.04 (s, 3H). LCMS Method O: retention time 1.45 min, [M+1] = 421.2. HPLC Method B: purity 98.7%, retention time 5.53 min.

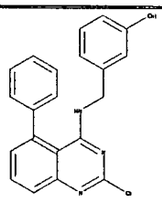
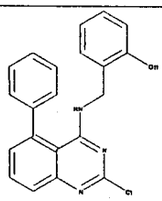
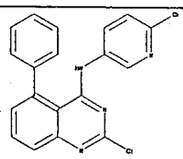
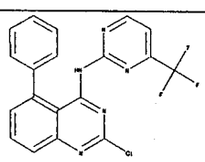
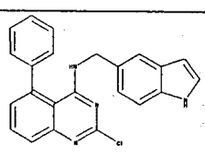
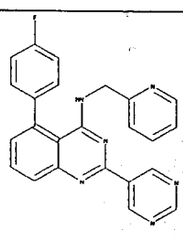
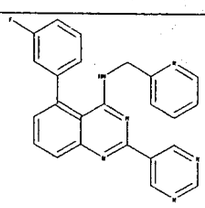
EXAMPLES 66 through 158

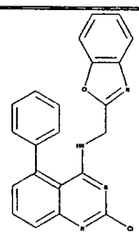
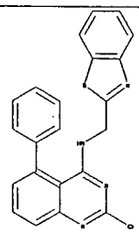
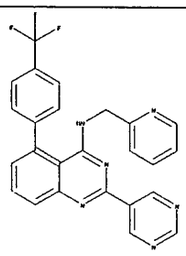
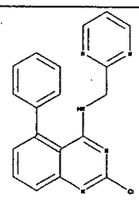
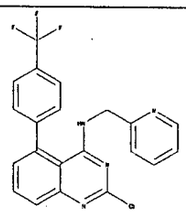
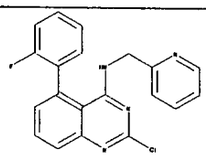
[00142] Examples 66 through 158 were synthesized via similar procedures described above. HPLC/MS data for each compound was collected using method E, and the molecular mass determined by MS (ES) by the formula m/z. Both the

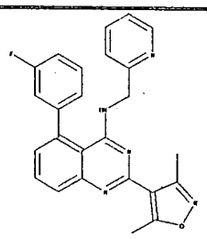
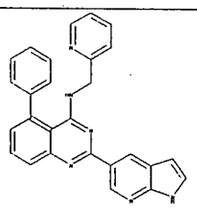
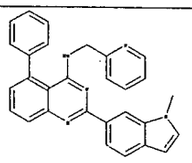
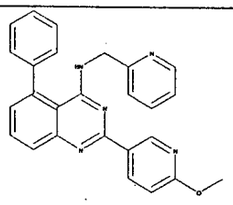
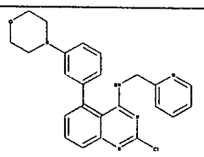
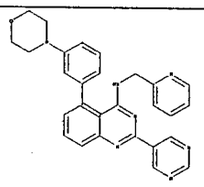
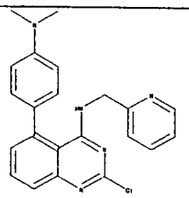
retention time and MS data for the examples are listed in Table 1b, wherein MW = molecular weight.

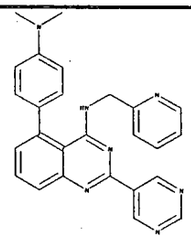
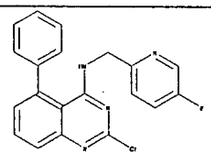
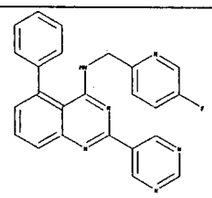
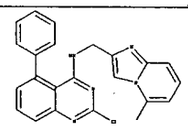
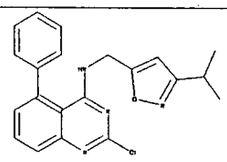
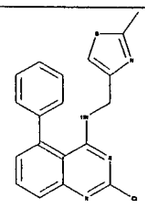
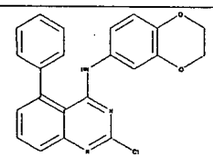
TABLE 1b

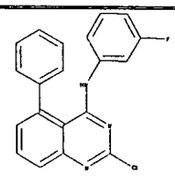
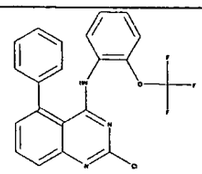
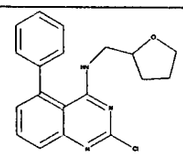
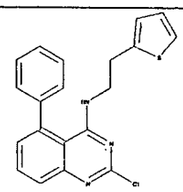
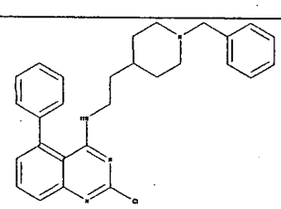
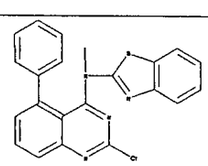
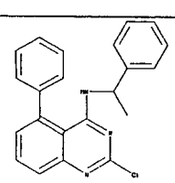
Example	Structure	MW	LCMS Data	LCMS Method
66		388.873	[M-1] 386.8 Rt: 5.82 min	L
67		480.967	[M] 478.7 Rt: 5.75 min	L
68		387.905	[M] 385.9 Rt: 7.09 min	L
69		438.93	[M-1] 436.9 Rt: 4.67 min	L
70		371.862	[M-1] 369.9 Rt: 6.68 min	L
72		388.893	[M] 386.9 Rt: 6.47 min	L
74		429.822	[M-1] 427.8 Rt: 6.83 min	L

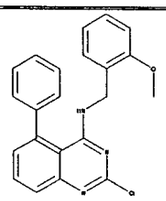
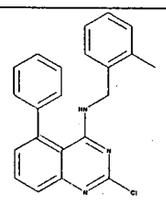
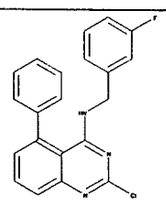
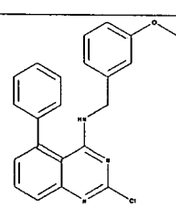
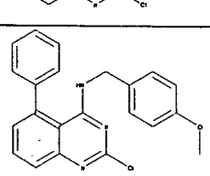
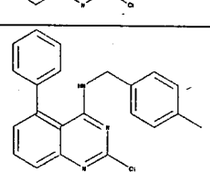
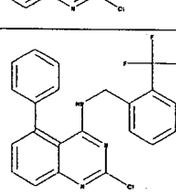
Example	Structure	MW	LCMS Data	LCMS Method
76		361.824	[M-1] 359.9 Rt: 5.06 min	L
77		361.824	[M-1] 359.8 Rt: 5.40 min	L
84		367.231	[M-1] 364.9 Rt: 6.09 min	L
85		401.772	[M-1] 399.8 Rt: 5.42 min	L
87		384.861	[M-1] 382.9 Rt: 5.72 min	L
88		408.43	[M+1] 409.2 Rt: 2.031 min	Q
89		408.43	[M+1] 409.2 Rt: 2.035 min	Q

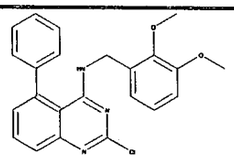
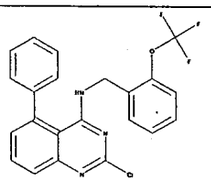
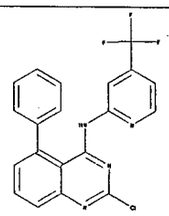
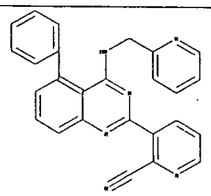
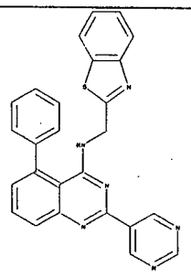
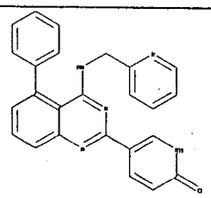
Example	Structure	MW	LCMS Data	LCMS Method
92		386.834	[M+1] 387.0 Rt: 2.102 min	O
93		402.899	[M+1] 403.0 Rt: 2.159 min	O
95		458.438	[M+1] 459.2 Rt: 3.225 min	S
96		347.801	[M+1] 348.2 Rt: 1.706 min	O
97		414.811	[M+1] 415.2 Rt: 2.016 min	Q
99		364.803	[M+1] 365.2 Rt: 2.010 min	Q

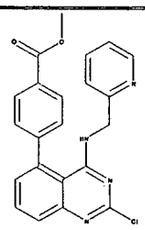
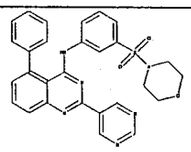
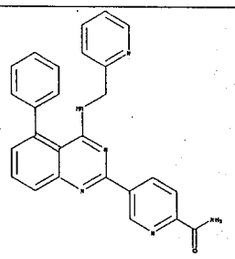
Example	Structure	MW	LCMS Data	LCMS Method
102		425.458	[M+1] 426.2 Rt: 3.298 min	S
103		428.488	[M+1] 429.2 Rt: 2.030 min	Q
104		441.526	[M+1] 442.2 Rt: 1.755 min	O
105		419.478	[M+1] 420.2 Rt: 3.957 min	R
106		431.917	[M+1] 432.2 Rt: 1.902 min	Q
107		475.544	[M+1] 476.2 Rt: 1.971 min	Q
108		389.881	[M+1] 390.2 Rt: 2.006 min	Q

Example	Structure	MW	LCMS Data	LCMS Method
109		433.508	[M+1] 434.2 Rt: 2.084 min	Q
110		364.803	[M+1] 365.0 Rt: 1.866 min	O
111		408.43	[M+1] 409.2 Rt: 2.099 min	Q
113		399.876	[M] 400.0 Rt: 3.09 min	L
114		378.855	[M] 379.0 Rt: 3.68 min	L
117		366.867	[M] 366.9 Rt: 3.32 min	L
118		389.834	[M] 388.2 Rt: 6.00 min	L

Example	Structure	MW	LCMS Data	LCMS Method
119		349.789	[M] 348.1 Rt: 6.48 min	L
122		415.796	[M-1] 414.1 Rt: 6.69 min	L
126		339.819	[M-1] 338.2 Rt: 5.28 min	L
127		365.879	[M-1] 364.2 Rt: 6.30 min	L
128		457.01	[M-1] 455.2 Rt: 5.07 min	L
129		402.899	[M-1] 401.1 Rt: 6.17 min	L
130		359.851	[M-1] 358.2 Rt: 6.46 min	L

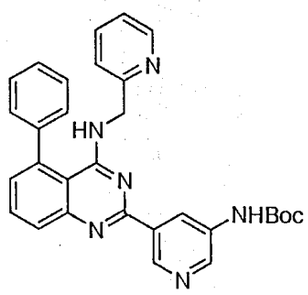
Example	Structure	MW	LCMS Data	LCMS Method
131		375.851	[M-1] 374.2 Rt: 6.31 min	L
132		359.851	[M-1] 358.1 Rt: 6.50 min	L
133		363.815	[M] 362.1 Rt: 6.16 min	L
134		375.851	[M-1] 374.2 Rt: 6.06 min	L
135		375.851	[M-1] 374.3 Rt: 6.06 min	L
136		359.851	[M-1] 358.2 Rt: 6.57 min	L
137		413.823	[M-1] 412.1 Rt: 6.59 min	L

Example	Structure	MW	LCMS Data	LCMS Method
138		405.877	[M+1] 406.1 Rt: 6.03 min	L
139		429.822	[M-1] 428.1 Rt: 6.76 min	L
143		400.784	[M-1] 399.1 Rt: 6.92 min	L
148		414.461	[M+1] 415.2 Rt: 1.685 min	O
149		446.526	[M+1] 447.0 Rt: 3.991 min	S
150		405.451	[M+1] 406.2 Rt: 1.347 min	O

Example	Structure	MW	LCMS Data	LCMS Method
152		404.849	[M+1] 405.2 Rt: 1.909 min	Q
154		524.594	[M+1] 525.2 Rt: 2.041 min	Q
158		432.477	[M+1] 433.0 Rt: 1.455 min	O

EXAMPLE 159

Tert-butyl 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-ylcarbamate

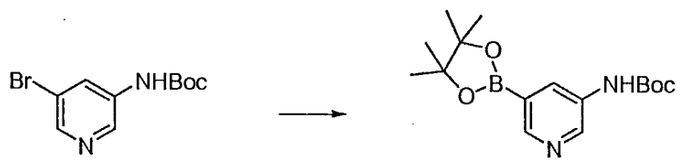


Step 1: Preparation of tert-butyl 5-bromopyridin-3-ylcarbamate

[00143] To 5-bromopyridin-3-amine (2.00 g, 11.5 mmol) in THF (25 mL) was added sodium hexamethyldisilazide (25.4 mL, 25.4 mmol, 1 M in THF) and the reaction mixture was stirred at room temperature for 20 min. Boc-anhydride (2.52 mL, 15.6 mmol) in THF (10 mL) was added slowly and the reaction mixture was

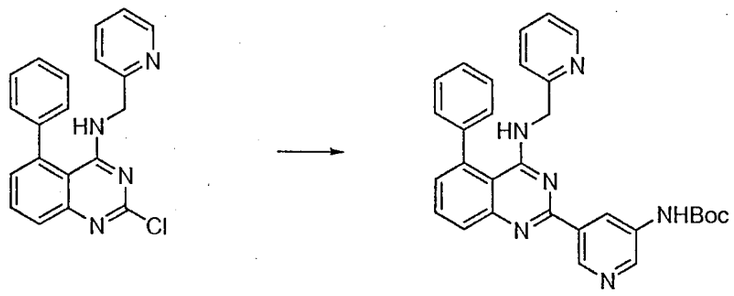
stirred for an additional 24 h at room temperature. 0.1 M HCl (30 mL) was added and the reaction mixture was extracted with ethyl acetate. The combined organic extracts were washed successively with water and brine. The organic layer was dried, filtered and concentrated under reduced pressure to afford tert-butyl 5-bromopyridin-3-ylcarbamate (2.5 g, 81 %), which was used without further purification. LCMS Method 0018: retention time 1.84 min, [M+1] = 275.0 ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.82 (s, 1H), 8.57 (d, 1H, J = 2.4Hz), 8.30 (d, 1H, J = 2Hz), 8.18 (s,1H), 1.49 (s, 9H).

Step 2: Preparation of tert-butyl 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-ylcarbamate



[00144] A mixture of tert-butyl 5-bromopyridin-3-ylcarbamate (0.8 g, 2.9 mmol), bis(pinacolato)diboron (0.82 g, 3.2 mmol) and potassium acetate (0.86 g, 8.7 mmol) in 1,4-dioxane (15 mL) was degassed with nitrogen for 15 min. After this time, (1,1'-Bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (0.12 g, 0.1 mmol) was added and the mixture was again degassed for 10 min. with nitrogen. Upon completion of this period, the reaction mixture was heated in the microwave at 120 ^{o}C for 45 min. After this time, the reaction mixture was filtered through celite and the filtrate was concentrated under reduced pressure to provide crude of tert-butyl 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-ylcarbamate (1.7 g), which was used without further purification.

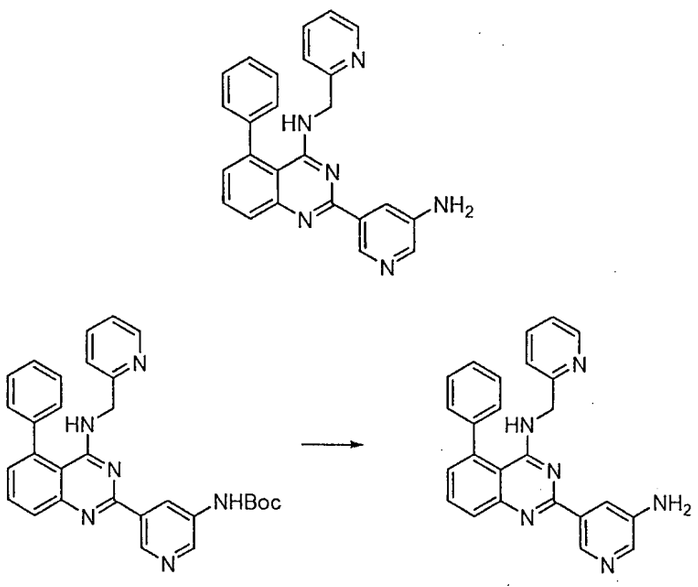
Step 3. Example 159



[00145] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (1.2 g, 3.4 mmol) in 1,4-dioxane (10 mL) and H_2O (2.5 mL) under nitrogen was added tert-butyl 5-(4;4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-ylcarbamate (1.7 g, 5.3 mmol), and potassium carbonate (1.4 g, 10 mmol). The mixture was degassed with nitrogen for 15 min. and then (1,1'-bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (0.25 mg, 0.3 mmol) was added. Upon completion of addition, the reaction mixture was again degassed for 10 min with nitrogen. After this time, the reaction mixture was stirred at 90 ^{O}C for 16 h, and then allowed to cool to room temperature. Once at the prescribed temperature, the reaction mixture was quenched by the addition of water and then transferred to a separation funnel. The aqueous layer was extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure to yield a residue. The residue was purified by silica gel column chromatography using a dichloromethane / methanol mixture to afford Example 159 (0.9 g, 52 % yield) as a brown solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.73 (br s, 1H); 9.25 (d, 1H, J = 2Hz); 8.95 (s, 1H); 8.76 (s, 1H); 8.25 (d, 1H, J = 4HZ); 7.91-7.80 (m, 2H); 7.73 (t, 1H, J = 8Hz); 7.60-7.50 (m, 5H); 7.39-7.29 (m, 2H); 7.25 (t, 1H, J = 10Hz); 6.83 (br s, 1H); 4.74 (d, 2H, J = 3.6 Hz); 1.54 (s, 9H). LCMS Method W: retention time 2.21 min; [M+1] = 505.2; HPLC Method K: purity 97.7%, retention time = 15.80 min.

EXAMPLE 160

2-(5-Aminopyridin-3-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine

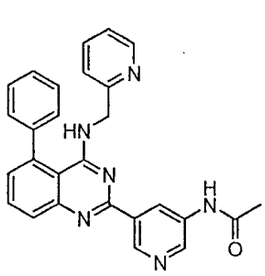


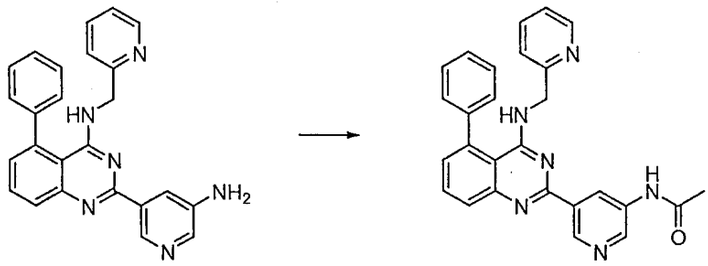
[00146] To a solution of Example 159 (750 mg, 1.48 mmol) in DCM (5 mL) at 0 °C was added 1.5 M HCl in dioxane (1.5 M). Upon completion of addition, the reaction mixture was stirred for 1 h and then concentrated to yield a residue. The residue was purified by combiflash using 3% methanol in DCM to give Example 160 (560 mg, 93 % yield) as an off white solid. ^{1}H NMR (400 MHz, DMSO-d6, δ): 8.84 (s, 1H); 8.24 (d, 1H, J = 3.6Hz): 8.04 (s, 1H); 8.00 (s, 1H); 7.89-7.79 (m, 2H); 7.72 (t, 1H, J = 7.2Hz); 7.62-7.48 (m, 5H); 7.35-7.22 (m, 3H); 6.78 (s, 1H); 5.47 (s, 2H); 4.73 (d, 12H, J = 3.6Hz); LCMS Method X: retention time 1.91min, [M+1] = 405.2

HPLC Method A1: purity 99.3%, retention time = 6.84 min.

EXAMPLE 161

N-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)acetamide

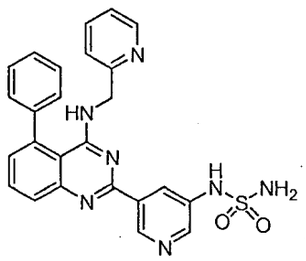


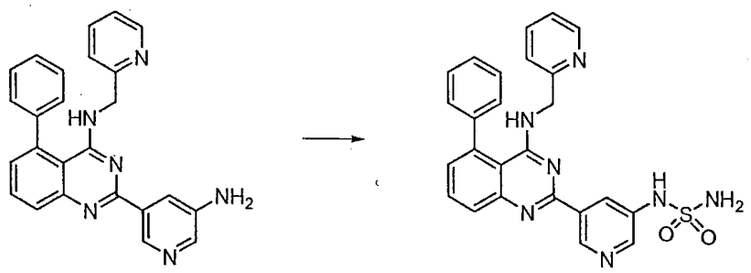


[00147] To a solution of Example 160 (0.2 g, 0.5 mmol) in acetone (20 mL) was added acetyl chloride (0.2 mL, 0.55 mmol) and potassium carbonate (0.2 g, 1.5 mmol). Upon completion of addition, the reaction mixture was stirred at room temperature for 4 h. After this time, the reaction mixture was filtered through celite, and the filtrate was concentrated to yield a residue. The residue was diluted with EtOAc and the organic portion was washed with saturated sodium bicarbonate (10 mL). The organic layer was dried, and then purified by silica gel column chromatography using dichloromethane / Methanol as the solvent to obtain Example 161 (180 mg, 82 %) as a white solid. ^{1}H NMR (400 MHz, DMSO-d6, δ): 10.34 (s, 1H); 9.31 (d, 1H, J = 2.4Hz); 8.96 (d, 2H, J = 5.2Hz), 8.24 (d, 1H, J = 4.8Hz), 7.93-7.80 (m, 2H), 7.73 (dt, 1H, J = 2.4Hz,7.6Hz), 7.60-7.47 (m, 5H), 7.38-7.28 (m, 2H), 7.24 (t, 1H, J = 9.2Hz), 6.85 (br s, 1H), 4.74 (d, 2H, J = 4Hz), 2.13 (s, 3H). LCMS Method W: retention time 1.85min, [M+1] = 447.2. HPLC Method A1: purity 98.5%, retention time = 7.20 min.

EXAMPLE 162

N-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl) sulfamide

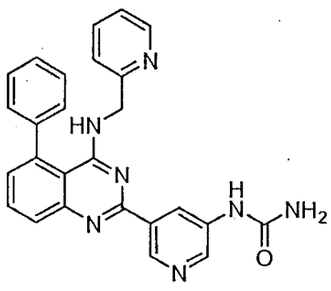


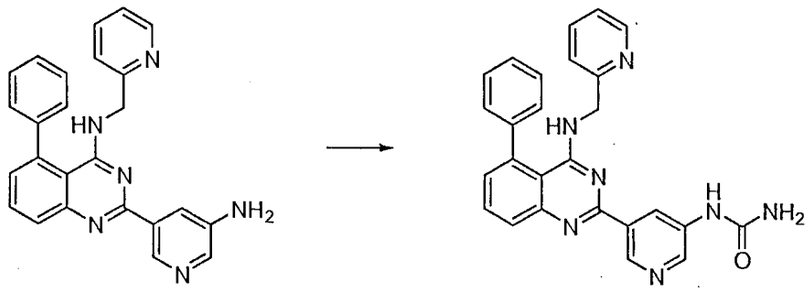


[00148] To a solution of chlorosulfonylisocyanate (0.021 mL, 0.24 mmol) in DCM (4 mL) was added t-BuOH (0.023 mL, 0.24 mmol) at RT. Upon completion of addition, the reaction mixture was stirred for 10 min. After this time, TEA was added (0.05 ml, 0.3 mmol), followed by a solution of Example 160 (0.1 g, 0.24 mmol) in DCM. The reaction mixture was stirred for an additional 3 h and then washed with a Na_2CO_3 solution. The aqueous layer was extracted with ethyl acetate. The combined organic extracts were dried, concentrated under reduced pressure and purified by silica gel column chromatography using dichloromethane / methanol mixture to yield Example 162 (0.040 g, 34 % yield). ^{1}H NMR (400 MHz, DMSO-d6, δ): 9.88 (s, 1H); 9.30 (s, 1H); 8.61 (br s, 1H); 8.56 (d, 1H, J = 2.4Hz); 8.24 (d, 1H, J = 4.4Hz); 7.91-7.80 (m, 2H); 7.73 (dt, 1H, J = 7.6Hz); 7.61-7.49 (m, 5H); 7.38-7.29 (m, 4H); 7.24 (t, 1H, J = 5.6Hz); 6.86 (br t, 1H, J = 3.6Hz); 4.74 (d, 2H, J = 4Hz). LCMS Method X: retention time 1.81min, [M+1] = 484.2. HPLC Method A1: purity 97.1%, retention time = 7.83 min.

EXAMPLE 163

1-(5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)urea

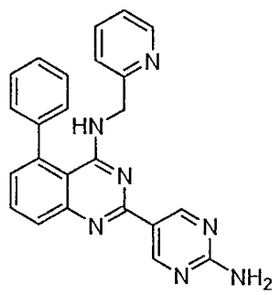


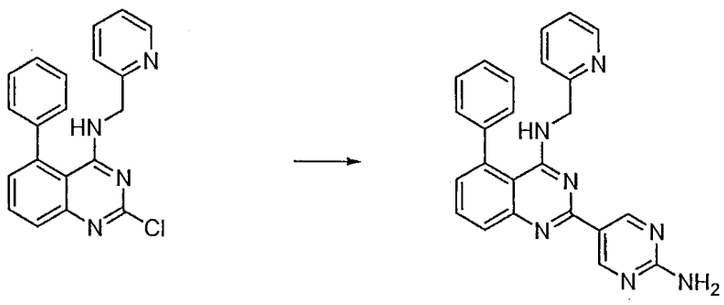


[00149] To a solution of Example 160 (0.2 g, 0.5 mmol) in DCM at 0 °C was added chlorosulfonylisocyanate (0.081 mL, 0.90 mmol). The resulting slurry was stirred at RT for 4 h and then 2 mL of 1.5 N HCl was added. Upon completion of addition, the reaction mixture was heated to 40 °C where it stirred for an additional 2 h. The resulting solution was neutralized with a sat. Na_2CO_3 solution and the aqueous portion was extracted with DCM. The combined organic extracts were dried, concentrated and purified by preparative HPLC 5 % methanol in dichloromethane to yield Example 163 (0.040 g, 18 % yield). ^{1}H NMR (400 MHz, DMSO-d6, δ): 9.19 (s, 1H); 8.94 (s, 1H); 8.83 (s, 1H); 8.76 (d, 1H, J = 2.4Hz); 8.24 (d, 1H, J = 4.8Hz); 7.90-7.80 (m, 2H); 7.73 (t, 1H, J = 8.4Hz); 7.60-7.50 (m, 5H); 7.38-7.29 (m, 2H); 7.24 (t, 1H, J = 5.2Hz); 6.83 (br t, 1H, J = 4Hz); 6.07 (br s, 2H); 4.74 (d, 2H, J = 4Hz). LCMS Method T: retention time 1.43 min, [M+1] = 448.0. HPLC Method A1: purity 98.8 %, retention time = 6.95 min.

EXAMPLE 164

2-(2-Aminopyrimidin-5-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine

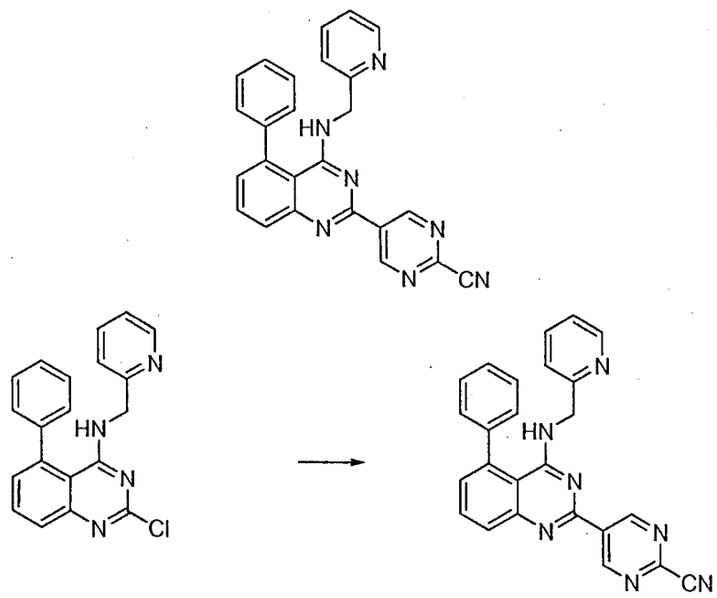




[00150] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.7 g, 2.02 mmol) in 1,4-dioxane (30 mL) and H_2O (5 mL) under nitrogen was added 2-aminopyrimidin-5-ylboronic ester (670 g, 3.03 mmol), and potassium carbonate (0.55 g, 4.04 mmol). Upon completion of addition, the mixture was degassed with nitrogen for 15 min and then (1,1'-bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (0.147 mg, 0.20 mmol) was added. The reaction mixture was again degassed for 10 min with nitrogen. After this time, the reaction mixture was heated to 90 °C where it stirred for 16 h. Aft the conclusion of this period, the reaction mixture was allowed to cool to room temperature and then quenched by the addition of water. The reaction mixture was transferred to a separation funnel and the aqueous layer was extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting concentrate was purified by silica gel column chromatography using dichloromethane / methanol mixture as the eluent to afford Example 164 (0.42 g, 52 % yield) as a brown solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.20 (s, 2H), 8.23 (d, 1H, J = 4.8 Hz), 7.78 (d, 2H, J = 2.4 Hz), 7.77-7.70 (m, 1H), 7.60-7.57 (m, 5H), 7.34-7.30 (m, 1H),7.26-7.20 (m, 2H), 7.18-7.13 (br s, 2H), 6.76 (br s, 1H), 4.67 (d, 2H, J = 4.0 Hz); LCMS Method U: retention time 1.38 min; [M+1] = 406; HPLC Method A1: purity 99.5 %, retention time = 6.74 min.

EXAMPLE 165

5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyrimidine-2-carbonitrile

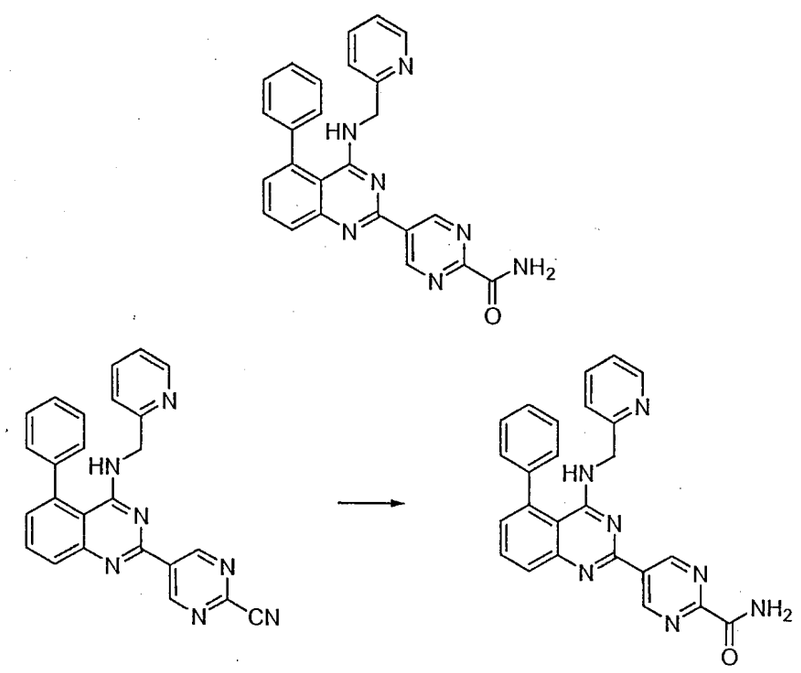


[00151] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.22 g, 0.65 mmol) in 1,4-dioxane (10 mL) and H_2O (2 mL) under nitrogen was added 2-cyanopyrimidin-5-ylboronic ester (0.22 g, 0.97 mmol), and potassium carbonate (0.18 g, 1.30 mmol). Upon completion of addition, the mixture was degassed with nitrogen for 15 min. After this time, (1,1'-bis(diphenylphosphino)-ferrocene)palladium (II) chloride dichloromethane complex (0.048 mg, 0.06 mmol) was added and the reaction mixture was again degassed with nitrogen for 10 min. After this time, the reaction mixture was stirred heated to 90 °C where it stirred for 16 h. At the conclusion of this period, the reaction mixture was allowed to cool to room temperature and then quenched by the addition of water. The reaction mixture was transferred to a separation funnel and the aqueous layer was extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting concentrate was purified by silica gel column chromatography using a dichloromethane / methanol mixture as the eluent to afford Example 165 (0.13 g, 49 % yield) as a brown solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.86 (s, 2H), 8.22 (d, 1H, J=6.4 Hz), 7.94 (dd, 1H, J=1.6 Hz J=8.4 Hz), 7.89 (dd, 1H, J= 3.2 Hz, J=11.2 Hz), 7.74 (dt, 1H, J=1.6 Hz, 8 Hz,), 7.63-7.50 (m, 5H),7.40-7.32 (m, 2H), 7.25 (dd, 1H, J=5.2 Hz, 6.8 Hz), 7.08 (br t, 1H, J= 4Hz), 4.76 (d, 2H, J=4.4 Hz).

LCMS Method U: retention time 1.85 min; [M+1] = 416.0; HPLC Method A4: purity 97.6%, retention time = 23.30 min.

EXAMPLE 166

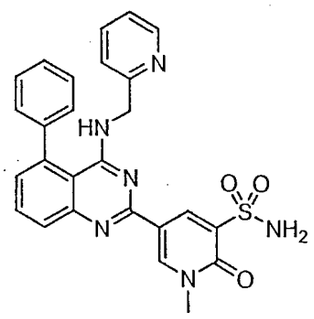
5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyrimidine-2-carboxamide



[00152] To a solution of Example 165 (0.115 g, 0.270 mmol) in THF was added NaOH (0.044 g, 1.1 mmol) and water. Upon completion of addition, the reaction mixture was cooled to 0 °C and hydrogen peroxide (0.037 g, 1.1 mmol) was added dropwise. The reaction mixture was stirred at RT for 2 h and then concentrated to yield a residue. The residue was diluted with water and the aqueous phase extracted with ethyl acetate. The combined organic extracts were dried and concentrated. The resulting residue was purified by Prep TLC using dichloromethane / methanol mixture as the eluent to yield Example 166 (0.075 g, 63 % yield). ^{1}H NMR (400 MHz, DMSO-d6, δ): 9.82 9s, 2H); 8.35 (d, 1H, J = 4Hz); 3.28 (s, 1H); 7.96 (dd, 1H, J = 0.8, 8.4Hz): 7.85 (t, 1H, J = 7.2Hz); 7.74 (dt, 1H, J = 1.4, 7.6Hz); 7.56-7.48 (m, 5H); 7.38 (dd, 1H, J = 0.8, 7.8Hz); 7.31-7.22 (m, 2H); 4.75 (d, 2H, J = 4Hz). LCMS Method Y: retention time 1.81 min, [M+1] = 434.2. HPLC Method A1: purity 96.1 %, retention time = 9.30 min.

EXAMPLE 167

1-Methyl-2-oxo-5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)-1,2-dihydropyridine-3-sulfonamide

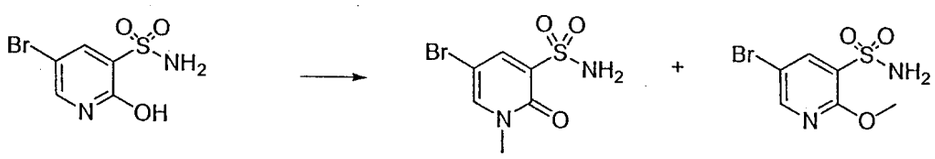


Step 1. Preparation of 5-bromo-2-hydroxypyridine-3-sulfonamide



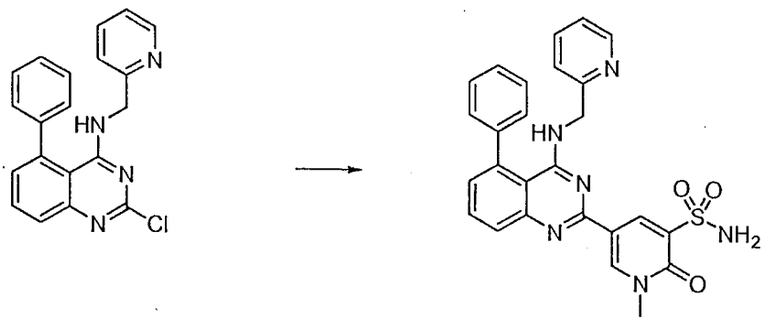
[00153] A solution of 5-bromopyridin-2-ol (0.5 g, 2.8 mmol) in chlorosulfonic acid (10 mL) was heated to 150 °C for 16 h. After this time, the reaction mixture was added dropwise to a pre-cooled aqueous ammonia solution (100 mL) at 0 °C. The resulting mixture was stirred for 1 h. The aqueous layer was then extracted with ethyl acetate (150 mL), dried and concentrated to yield a residue. The residue was purified by ISCO chromatography using 3 % methanol in DCM to yield 5-bromo-2-hydroxypyridine-3-sulfonamide (210 mg). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.67 (br s, 1H); 8.03 (d, 1H, J = 2.8Hz); 7.98 (d, 1H, J = 2.8Hz); 7.11 (s, 1H). LCMS Method U: retention time 1.85 min; [M+1] = 253.0.

Step 2. Preparation of 5-bromo-2-methoxypyridine-3-sulfonamide



[00154] To a solution of 5-bromo-2-hydroxypyridine-3-sulfonamide (0.5 g, 1.9 mmol) in MeOH/DCM (15 mL, 1:1) at -10 °C was added trimethylsilyldiazomethane solution (2 M, 1.97 mL, 3.9 mmol). Upon completion of addition, the reaction mixture was concentrated and the resulting residue was purified by column chromatography using methanol and $CHCl_3$ to 5-bromo-1-methyl-2-oxo-1,2-dihydropyridine-3-sulfonamide yield 5-bromo-1-methyl-2-oxo-1,2-dihydropyridine-3-sulfonamide (280 mg, 53 % yield) and 5-bromo-2-methoxypyridine-3-sulfonamide (180 mg, 34 % yield). Data for 5-bromo-1-methyl-2-oxo-1,2-dihydropyridine-3-sulfonamide: ^{1}H NMR (400 MHz, DMSO-d6, δ): 8.42 (d, 1H, J = 2.8Hz); 7.99 (d, 1H, J = 2.8Hz); 7.14 (s, 1H); 3.52 (s, 3H). Data for 5-bromo-2-methoxypyridine-3-sulfonamide: ^{1}H NMR (400 MHz, DMSO-d6, δ): 8.54 (d, 1H, J = 2.4Hz); 8.17 (d, 1H, J = 2.4Hz); 7.51 (s, 1H); 4.00 (s, 3H).

Step 3: Example 167

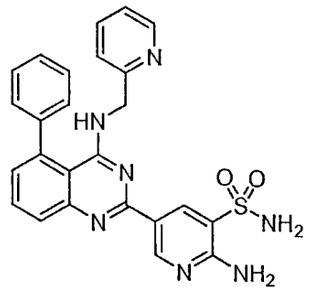


[00155] A stirred solution of 5-bromo-1-methyl-2-oxo-1,2-dihydropyridine-3-sulfonamide (0.08 g, 0.3 mmol) in dioxane:DMF (6 mL: 1 mL) was degassed for 10 min with argon. At the conclusion of this period, Pd(triphenylphosphine)$_4$ (34 mg, 0.03 mmol) and hexamethylditin (0.17 g, 0.53 mmol) were added. The reaction mixture was stirred at room temperature for 16 h. and then 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.1 g, 0.3 mmol) was added. Upon completion of addition, the reaction mixture was heated to 100 °C where it stirred for an additional 16 h. A precipitate was formed and the resulting slurry was filtered. The filtrate was concentrated and purified by silica gel column chromatography using dichloromethane / methanol mixture as the eluent to obtain Example 167 (15 mg, 13 % yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.06 (s, 1H); 9.02 (s, 1H); 8.25

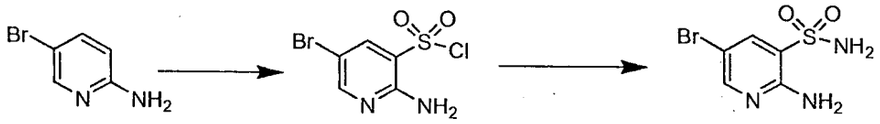
(d, 1H, J = 4Hz); 7.86-7.78 (m, 2H); 7.73 (dt, 1H, J = 1.6, 7.6Hz); 7.60-7.48 (m, 5H); 7.31-7.22 (m, 3H); 7.09 (br s, 2H); 6.79 (t, 1H, J =4Hz); 4.72 (d, 2H, J = 4Hz); 3.72 (s, 3H). LCMS Method U: retention time 1.35 min; [M+1] = 499.2; HPLC Method A1: purity 96.2 %, retention time = 6.10 min.

EXAMPLE 168

2-Amino-5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridine-3-sulfonamide

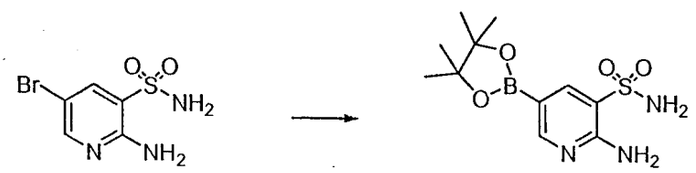


Step 1. Preparation of 2-amino-5-bromopyridine-3-sulfonamide



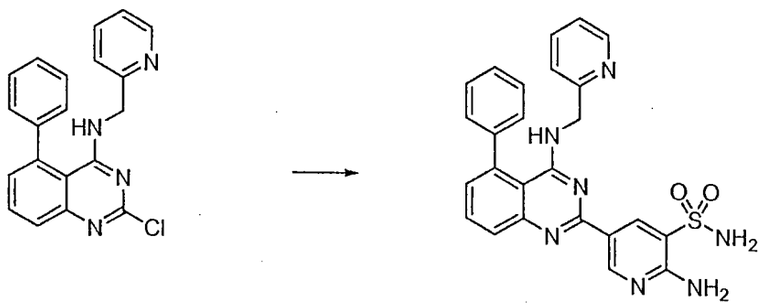
[00156] To a solution of chlorosulfonic acid (20 mL) at 0 °C was added 2-amino-5-bromopyridine (5.0 g, 0.029 mmol) portion wise. Upon completion of addition, the reaction mixture was heated to reflux where it stirred for 16 h. After this time, the reaction mixture was allowed to cool to RT. Once at the prescribed temperature, the reaction mixture was poured drop wise in to an aqueous ammonium hydroxide solution. The resulting mixture was extracted with ethyl acetate. The combined organic portions were washed with a brine solution, dried over Na_2SO_4 and concentrated under reduced pressure to yield 2-amino-5-bromopyridine-3-sulfonamide (4.7 g, 65 %), which was used without further purification. LCMS Method Y: retention time 0.5 min, [M-1] = 250.8.

Step 2. Preparation of 2-amino-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine-3-sulfonamide which was used without further purification



[00157] A mixture of 5-bromo-2-aminopyridine-3-sulfonamide (2.0 g, 7.9 mmol), bis(pinacolato)diboron (3.0 g, 12 mmol) and potassium acetate (2.3 g, 23 mmol) in 1,4-dioxane (20 mL) was degassed with nitrogen for 15 min. After this time, (1,1'-bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (0.29 g, 0.36 mmol) was added and the reaction mixture was again degassed for 10 min with nitrogen. The reaction mixture was heated to 100 °C where it stirred for 12 h. At the conclusion of this period, the reaction mixture was filtered through celite and the filtrate was concentrated under reduced pressure to provide 2-amino-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine-3-sulfonamide (1 g), which was used without further purification. LCMS Method X: retention time 1.29 min; [M+1] = 300.

Step 3. Example 168

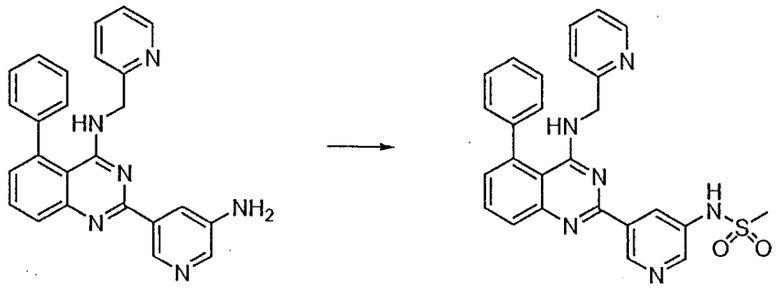


[00158] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.20 g, 0.57 mmol) in 1,4-dioxane (5 mL) and H_2O (0.55 mL) under nitrogen was added 2-amino-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine-3-sulfonamide (0.259, 0.800 mmol), and potassium carbonate (0.239 g, 1.70 mmol). Upon completion of addition, the reaction mixture was degassed with nitrogen for 15 min. After this time, (1,1'-bis(diphenylphosphino)ferrocene)palladium (II) chloride

dichloromethane complex (0.023 mg, 0.020 mmol) was added and the resulting mixture was again degassed for 10 min with nitrogen. The reaction mixture was heated to 90 °C where it stirred for 16 h. At the conclusion of this period, the reaction mixture was allowed to cool to room temperature. Once at the prescribed temperature, the reaction mixture was quenched by the addition of water. The reaction mixture was transferred to a separation funnel and the aqueous layer was extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting concentrate was purified by silica gel column chromatography using dichloromethane / methanol mixture as the eluent and further purified by preparative HPLC using 7 % methanol in dichloromethane as the eluent to afford Example 168 (0.060 g, 22 % yield) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.14 (d, 1H, J = 2.4Hz); 9.02 (d, 1H, J = 2.4Hz); 8.37 (d, 1H, J = 3.6Hz); 7.87 (dd, 1H, J = 1.2, 8.4Hz): 7.82-7.72 (m, 2H); 7.58-7.47 (br s, 5H), 7.35-7.23 (m, 3H); 4.71 (s, 2H). LCMS Method Y: retention time 1.87 min; [M+1] = 484.2; HPLC Method A2: purity 98.1 %, retention time = 12.93 min. Preparative HPLC Method-I.

EXAMPLE 169

N-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)methane sulfonamide

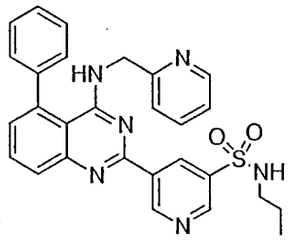


[00159] To a stirred solution of 2-(5-aminopyridin-3-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (Example 161: 0.12 g, 0.3mmol) and TEA (0.080 mL, 0.45 mmol) in DCM (10 mL) at RT was added methanesulfonyl chloride (0.30 mL, 0.44 mmol) dropwise at 0 °C and the reaction mixture was stirred at RT for 2 h. The reaction mixture was diluted with water and the resulting solution extracted with

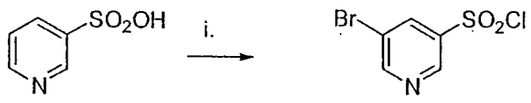
DCM. The combined organic extracts were washed successively with water and brine dried, filtered and the filtrate concentrated. The residue was purified by silica gel column chromatography using dichloromethane/methanol mixture (98/2) as the eluent to provide Example 169 (65 mg, 45 % yield) as an off white solid. ^{1}H NMR (400 MHz, DMSO-d6, δ): 10.35 (br s, 1H); 9.40 (s, 1H); 8.68 (s, 1H), 8.58 (s, 1H), 7.24 (d, 1H, J = 3.2Hz), 7.90-7.82 (m, 2H), 7.73 (dd, 1H, J = 1.2Hz, 7.2Hz), 7.62-7.50 (m, 5H), 7.34-7.30 (m, 2H), 7.23 (t, 1H, J = 5.2Hz), 6.85 (t, 1H, J = 4Hz), 4.73 (d, 2H, J = 4Hz), 3.11 (s, 3H). LCMS Method Y: retention time 1.89min, [M+1] = 483.2
HPLC Method A1: purity 97.8%, retention time = 6.61 min.

EXAMPLE 170

N-(2-methoxyethyl)-5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridine-3-sulfonamide



Step 1. Preparation of 5-bromopyridine-3-sulfonyl chloride.



[00160] A mixture of pyridine-3-sulfonic acid (10.3 g, 64.8 mmol), phosphorous pentachloride (20.8 g, 100 mmol) and phosphorous oxychloride (10 mL, 100 mmol) was heated at reflux for 4 h. The reaction mixture was allowed to cool to room temperature and evaporated to dryness under reduced pressure. The residue was treated with bromine (6.00 mL, 116 mmol) and heated at reflux for 14 h. The reaction mixture was cooled to 0 °C then slowly quenched by the addition of ice water. The resulting mixture was diluted with ethyl acetate, the organic layer separated and the

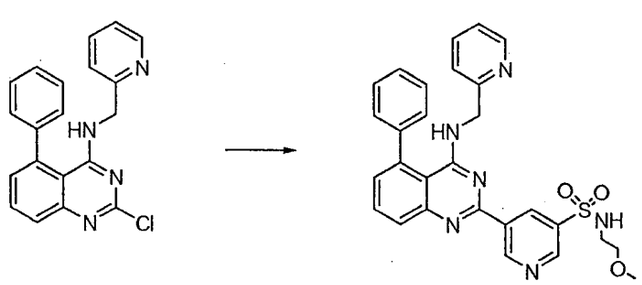
aqueous layer extracted further with ethyl acetate. The combined organic layers were dried over Na_2SO_4 then concentrated to afford 5-bromopyridine-3-sulfonyl chloride (5.0 g) as a semi solid, which was used without further purification.

Step 2. Preparation of 5-bromo-N-(2-methoxyethyl)pyridine-3-sulfonamide.



[00161] A solution of 5-bromopyridine-3-sulfonyl chloride (1.5 g, 5.8 mmol)) and 2-methoxyethanamine (1.3 g, 18 mmol) in THF (40 mL) was stirred at room temperature for 16 h. After this time, the resulting reaction mixture was partitioned between saturated aqueous sodium chloride and ethyl acetate. The organic solution was dried and evaporated. The resulting residue was purified by flash column chromatography using ethyl acetate/hexanes to yield 5-bromo-N-(2-methoxyethyl)pyridine-3-sulfonamide (460 mg, 27 %). LCMS Method T: Retention time 1.13 min; [M+1] =295, 297.

Step 3. Example 170

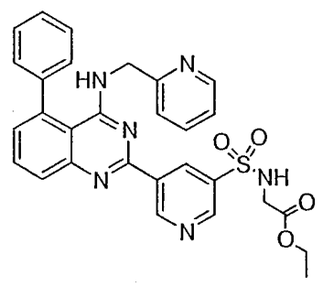


[00162] A stirred solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.15 g, 0.43 mmol) in dioxane (10 mL) was degassed for 10 min with argon and Pd(TRIPHENYLPHOSPHINE)$_4$ (0.05 g, 0.043 mmol) and hexamethylditin (0.25 g, 0.77 mmol) were added and the reaction mixture stirred at room temperature for 16 h. 5-bromo-N-(2-methoxyethyl)pyridine-3-sulfonamide (0.19 g, 0.65 mmol) was

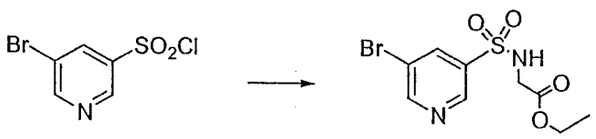
added to the reaction mixture and the resulting solution heated at 100 °C for an additional 16 h. A precipitate formed and the solids were filtered from the reaction mixture and filtrate concentrated and purified by silica gel column chromatography using dichloromethane / methanol mixture as the eluent to yield Example 170 (0.065 g, 27 %) as an off white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.83 (s,1H), 9.11 (s.1H), 9.06 (s,1H), 8.24 (br s.1H), 8.19 (t, 1H, J=5.6), 7.97-7.92 (m,1H), 7.88 (t, 1H, J = 4), 7.73 (t, 1H, J = 8), 7.63-7.50 (m, 5H), 7.38-7.30 (m, 2H), 7.25 (t, 1H), 6.96 (br s, 1H), 4.76 (d, 2H, J = 4.4), 3.34-3.30 (m, 2H), 3.11 (s, 3H), 3.05 (t, 2H, J = 5.6). LCMS Method T: retention time 1.61 min; [M+1] = 527. HPLC Method A1: purity 99.4 %, retention time = 8.17 min.

EXAMPLE 171

Ethyl 2-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridine-3-sulfonamido)acetate



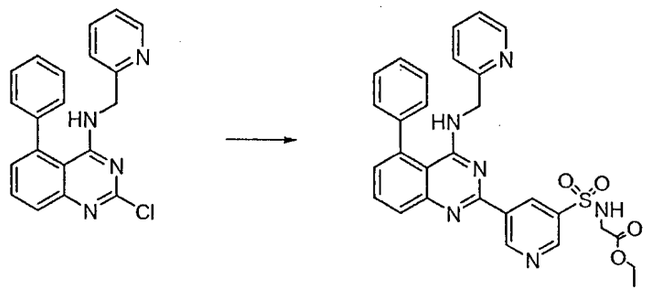
Step 1. Preparation of ethyl 2-(5-bromopyridine-3-sulfonamido)acetate



[00163] A solution of 5-bromopyridine-3-sulfonyl chloride (3.5 g, 14 mmol) (described in the synthesis of Example 170) and glycine ethylester (2.1 g, 20 mmol), diisopropyl ethyl amine (2.6 g, 20 mmol) in THF (70 mL) was stirred at room temperature for 16 h. The reaction mixture was partitioned between saturated aqueous sodium chloride and ethyl acetate. The organic solution was separated, dried and evaporated under reduced pressure. The residue was purified using flash column chromatography using ethyl acetate/hexanes as eluent to obtain ethyl 2-(5-

bromopyridine-3-sulfonamido)acetate (600 mg, 14 %). LCMS Method I: retention time 1.31min; [M+1] = 323,325.

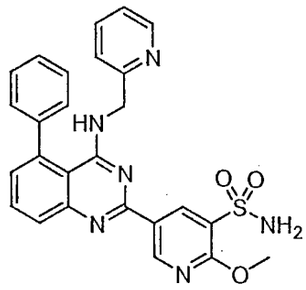
Step 2. Example 171



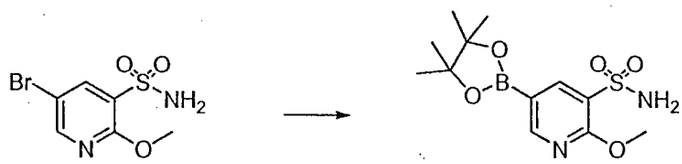
[00164] To a solution of methylethyl 2-(5-bromopyridine-3-sulfonamido)acetate (0.20 g, 0.62 mmol) in dioxane (10 mL) was added hexamethylditin (0.30 g, 0.92 mmol) and LiCl (26 mg, 0.62 mmol). The reaction mixture was degassed with nitrogen for 10 min and then charged with Tetrakis triphenyl phosphine palladium (68 mg, 0.061 mmol). The reaction mixture was stirred for 5 h at room temperature under nitrogen atmosphere. After this time, 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.17 g, 0.50 mmol) in dioxane (2 mL) was added drop wise and the reaction mixture was heated to reflux for 18 h. The reaction mixture was quenched by the addition of water and extracted with ethyl acetate. The combined organic extracts were washed successively with water and brine, dried, filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel using 5% methanol in dichloromethane to afford Example 171 (35mg, 11%) as an off white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.82 (s, 1H); 9.10 (s, 1H); 9.06 (s, 1H); 8.68 (t, 1H, J = 6.0Hz); 8.24 (d, 1H, J = 4.8Hz); 7.94 (dd, 1H, J = 1.2, 8.0Hz); 7.86 (t, 1H, 5.6Hz); 7.73 (dt, 1H, J = 1.6, 8.0Hz); 7.62-7.50 (m, 5H); 7.33-7.36 (m, 2H); 7.26-7.23 (m, 1H); 6.96 (s, 1H); 4.76 (d, 2H, J = 4Hz); 3.93 (q, 2H, J = 7.2Hz); 3.89 (d, 2H, J = 6.0Hz); 1.04 (t, 3H, J = 7.2Hz). LCMS Method U: retention time 1.65 min; [M+1] = 555.2; HPLC Method A4: purity 98.9%, retention time = 9.15 min.

EXAMPLE 172

2-Methoxy-5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridine-3-sulfonamide

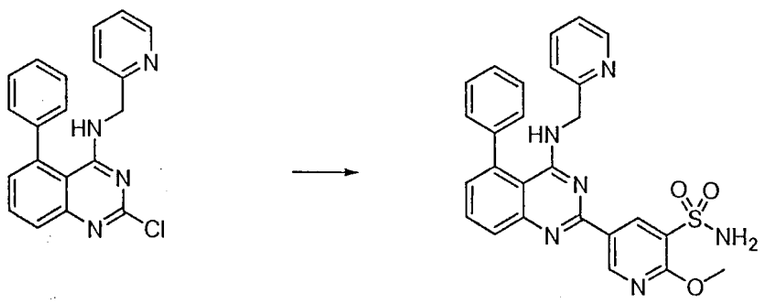


Step 1. Preparation of 2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine-3-sulfonamide



[00165] A mixture of 5-bromo-2-methoxypyridine-3-sulfonamide (described in the synthesis of Example 167: 0.15 g, 0.56 mmol), bis(pinacolato)diboron (0.17 g, 0.6 mmol) and potassium acetate (0.22 g, 2.2 mmol) in 1,4-dioxane (10 mL) was degassed with nitrogen for 15 min. After this time, (1,1'-bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (0.036 g, 0.04 mmol) was added and the reaction mixture was again degassed for 10 min. with nitrogen. The reaction mixture was heated in the microwave at 120 °C for 45 min. The reaction mixture was filtered through celite and the filtrate was concentrated under reduced pressure to provide 2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine-3-sulfonamide (0.15 g), which was used without further purification. LCMS Method T: retention time 0.44 min; [M+1] = 233.0.

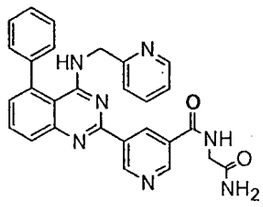
Step 2. Example 172



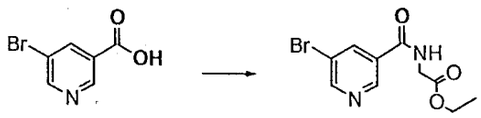
[00166] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.19 g, 0.5 mmol) in 1,4-dioxane (5 mL) and H_2O (0.55 mL) under nitrogen was added 2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine-3-sulfonamide (0.15 g, 0.60 mmol), and potassium carbonate (0.22 g, 1.6 mmol). The reaction mixture was degassed with nitrogen for 15 min. (1,1'-bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (0.22 mg, 0.02 mmol) was added and the reaction mixture was again degassed for 10 min with nitrogen. The reaction mixture was stirred at 90 °C for 16 h, then allowed to cool to room temperature and quenched by the addition of water. The reaction mixture was transferred to a separation funnel and the aqueous layer extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The concentrate was purified by column chromatography to afford Example 172 (0.060 g, 22 % yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.78 (br s, 1H); 9.03 (d, 1H, J = 2Hz); 8.66 (s, 1H); 8.24 (d, 1H, J = 4.8Hz); 7.86-7.75 (m, 2H); 7.71 (t, 1H, J = 7.6Hz); 7.60-7.46 (m, 5H); 7.30-7.20 (m, 3H); 7.07 (br s, 2H); 6.80 (br s, 1H); 4.67 (d, 2H, J = 4Hz). LCMS Method U: retention time 1.32 min; [M+1] = 485.0; HPLC Method A4: purity 97.1 %, retention time = 5.91 min.

EXAMPLE 173

N-(2-amino-2-oxoethyl)-5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinamide

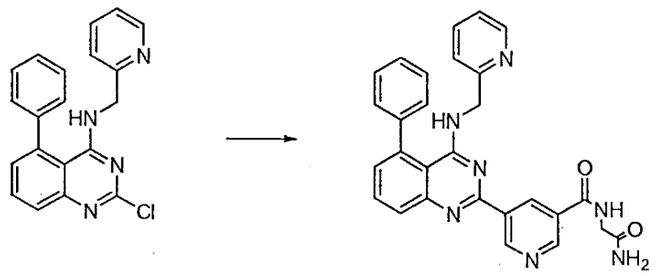


Step 1. Preparation of ethyl 2-(5-bromonicotinamido)acetate



[00167] A solution of 5-bromonicotinic acid (4 g, 0.02 mol) in thionyl chloride (25 mL) was heated under reflux for 4 h. The excess thionyl chloride was removed under reduced pressure to provide 5-bromonicotinyl chloride which was used without further purification. To 5-bromonicotinyl chloride (3.5 g, 13.6 mmol) was added glycine ethylester (2.1 g, 20.3 mmol) and diisopropyl ethyl amine (2.6 g, 20.1 mmol) in THF (70 mL) and the reaction mixture stirred at RT for 16 h. The reaction mixture was diluted with EtOAc and washed with brine solution. The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure and the residue was purified by silica gel column chromatography using 25 % EtOAc in hexane to provide ethyl 2-(5-bromonicotinamido)acetate 1.2 g (33 %) as a brown solid. LCMS Method T: retention time 1.28 min; [M+1] = 288.2

Step 2. Preparation of Example 173

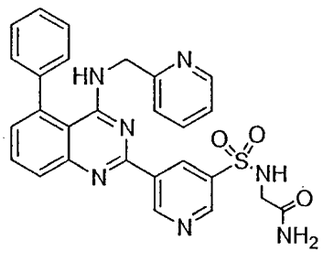


[00168] To a solution of N-(2-amino-2-oxoethyl)-5-bromonicotinamide (0.220 g, 0.852 mmol) in dioxane (4 mL), was added hexamethylditin (0.50 g, 1.53 mmol). The reaction mixture was degassed with nitrogen for 15 min. Pd(triphenylphosphine)$_4$

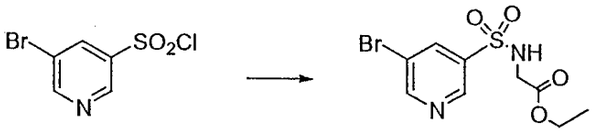
(0.098 g, 0.08 mmol) was added and the reaction mixture was stirred at RT for 6 h. 2-Chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.29 g 0.84 mmol) in 1,4-dioxane (3 mL) was added and the resulting mixture was stirred at 95 °C for 16 h, allowed to cool to room temperature and then quenched by the addition of water. The reaction mixture was transferred to a separation funnel and the aqueous layer extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The concentrate was purified by silica gel column chromatography using dichloromethane / methanol mixture as the eluent to yield Example 173 (12 mg, 4 %) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.76 9s, 1H); 9.21 (s, 1H); 9.16 (s, 1H); 9.14-9.11 (m, 1H); 8.24 (d, 1H, J = 4.4Hz); 7.94 (d, 1H, J = 4.4Hz); 7.86 (t, 1H, J = 7.6Hz): 7.73 (dd, 1H, J = 7.6, 15.2Hz); 7.68-7.47 (m, 5H); 7.39-7.30 (m, 2H); 7.24 (dd, 1H, J = 5.2, 7.6Hz); 7.10 (br s, 1H); 6.93 (br s, 1H); 4.77 (d, 2H, J = 4Hz); 3.90 (d, 2H, J = 5.6Hz). LCMS Method Y: retention time 1.70 min; [M+1] = 490.2; HPLC Method A1: purity 99.5%, retention time = 5.73 min.

EXAMPLE 174

2-(5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridine-3-sulfonamido)acetamide

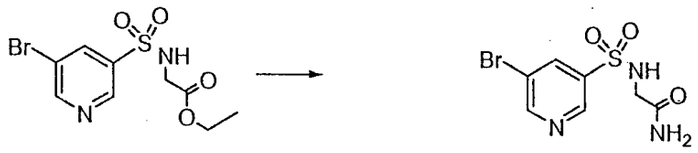


Step 1. Preparation of ethyl 2-(5-bromopyridine-3-sulfonamido)acetate



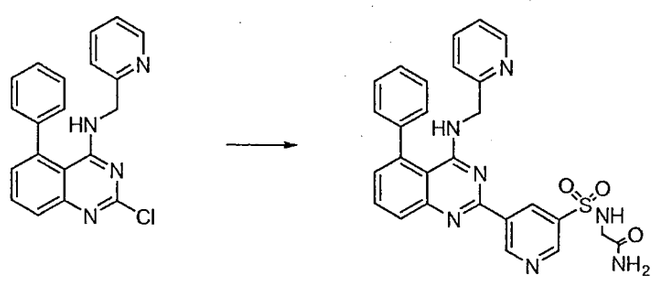
[00169] A solution of 5-bromopyridine-3-sulfonyl chloride (3.5 g, 14 mmol) and glycine ethylester (2.1 g, 20 mmol), diisopropyl ethyl amine (2.6 g, 20 mmol) in THF (70 mL) was stirred at room temperature for 16 h. The reaction mixture was partitioned between saturated aqueous sodium chloride and ethyl acetate. The organic solution was separated, dried and evaporated under reduced pressure. The residue was purified using flash silica gel column chromatography using ethyl acetate/hexanes to obtain ethyl 2-(5-bromopyridine-3-sulfonamido)acetate (600 mg, 14 %); LCMS Method T: retention time 1.31min; [M+1] = 323,325.

Step 2. Preparation of 2-(5-bromopyridine-3-sulfonamido)acetamide



[00170] A solution of ethyl 2-(5-bromopyridine-3-sulfonamido)acetate (0.50 g, 1.7 mmol) and ammonia in methanol (2M, 10 mL) was heated to 60 °C in a sealed tube for 4 h. The cooled reaction mixture was concentrated under reduced pressure to yield 2-(5-bromopyridine-3-sulfonamido)acetamide (300 mg, 66 %), which was used without further purification. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.96 (d, 1H, J = 2.4Hz); 8.90 (d, 1H, J = 2Hz); 8.39 (t, 1H, J =2Hz), 8.21 (br s, 1H), 7.35 (br s, 1H), 7.07 (br s, 1H), 3.5 (s,2H). LCMS Method D: retention time 0.945 min; [M+1] = 294,296.0.

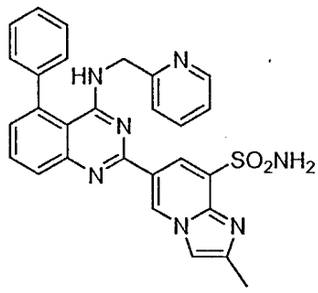
Step 3. Example 174



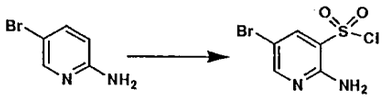
[00171] A stirred solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.20 g, 0.57 mmol) in dioxane (10 mL) was degassed for 10 min with argon and Pd(TRIPHENYLPHOSPHINE)$_4$ (0.06 g, 0.05 mmol) and hexamethylditin (0.34 g, 1.03 mmol) were added and the resulting reaction mixture was stirred at room temperature for 16 h. 2-(5-bromopyridine-3-sulfonamido)acetamide (0.25 g, 0.86 mmol) was added to the above reaction mixture and the solution heated at 100 °C for an additional 16 h. A precipitate formed and the solids were filtered from the reaction mixture and filtrate concentrated and purified by column chromatography to yield Example 174 (0.060 g, 20 %) as a brown solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.80 (s, 1H), 9.11 (s, 1H), 9.05 (s, 1H), 8.25 (d, 1H, J = 4.8 Hz), 7.95 (dd, 1H, J =1.2 Hz, J =8.4 Hz), 7.86 (t, 1H, J = 8.8 Hz),7.73 (t, 1H, J = 4.4 Hz), 7.61-7.50 (m, 5H), 7.40-7.32 (m, 3H), 7.26-7.24 (m, 1H), 7.07 (br s, 1H), 6.97 (br t, 1H, J = 3.6 Hz), 4.76 (d, 2H, J = 4 Hz), 3.56 (s, 2H). LCMS Method Y: retention time 1.77 min; [M+1] = 526.0; HPLC Method A1: purity 99.2%, retention time = 6.709 min.

EXAMPLE 175

2-Methyl-6-(5-phenyl-4-(yridine-2-ylmethylamino)quinazolin-2-yl)imidazo[1,2-a]pyridine-8-sulfonamide



Step 1. Preparation of 2-amino-5-bromopyridine-3-sulfonyl



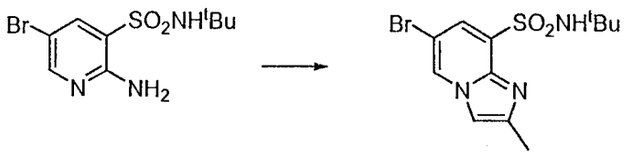
[00172] To a cooled (0 °C) solution of chlorosulfonic acid (58 mL) under vigorous stirring was added 5-bromo-2-pyridinamine (86.7 mmol) portion wise. The reaction mixture was then heated at reflux for 3 h. Upon cooling to room temperature, the reaction mixture was poured over ice (100 g) with vigorous stirring. The resulting yellow precipitate was collected by suction filtration, washed with cold water and petroleum ether to provide 2-amino-5-bromopyridine-3-sulfonyl chloride (18 g, 77% yield) as an orange-yellow solid.

Step 2. Preparation of 2-amino-5-bromo-N-tert-butylpyridine-3-sulfonamide



[00173] 2-amino-5-bromopyridine-3-sulfonyl chloride (15 g, 55 mmol) was dissolved in THF (125 mL) and at 0 °C t-butylamine (6.5 g, 111 mmol) was added and the reaction mixture was stirred at RT for 2 h. The reaction mixture was concentrated under reduced pressure to yield 2-amino-5-bromo-N-tert-butylpyridine-3-sulfonamide (8.4 g, 49 %), which was used without further purification. LCMS Method Y: retention time 1.70 min, [M-1] = 306.0.

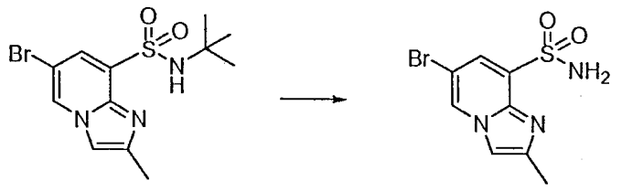
Step 3. Preparation of 6-bromo-N-tert-butyl-2-methylimidazo[1,2-a]pyridine-8-sulfonamide



[00174] To a solution of 2-amino-5-bromo-N-tert-butylpyridine-3-sulfonamide (3.0 g, 9.7 mmol) in ethanol (6 mL) was added chloroacetone (3.0 mL, 48 mmol) and the reaction mixture was stirred at 80 °C for 48 h. The solvents were evaporated under reduced pressure and the residue was purified by flash silica gel column chromatography (5 % methanol in DCM) to yield 6-bromo-N-tert-butyl-2-

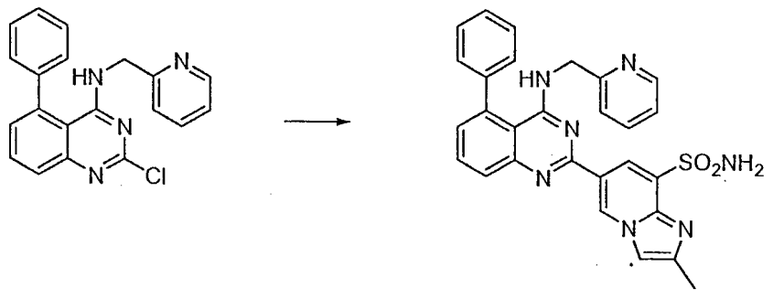
methylimidazo[1,2-a]pyridine-8-sulfonamide (2.2 g, 66 %), which was used without further purification. LCMS Method T: retention time 1.33 min; [M+1] = 346.64.

Step 4. Preparation of 6-bromo-2-methylimidazo[1,2-a]pyridine-8-sulfonamide



[00175] 6-bromo-N-tert-butyl-2-methylimidazo [1, 2-a] pyridine-8-sulfonamide (1.0 g, 2.8 mmol) was stirred in TFA (6 mL) for 16 h. The TFA was removed in vacuo and a saturated solution of $NaHCO_3$ was added. The aqueous layer was extracted with DCM, the combined organic portions dried, filtered and concentrated to yield 6-bromo-2-methylimidazo[1,2-a]pyridine-8-sulfonamide (0.45 g, 54 %), which was used without further purification. LCMS Method Y: retention time 1.44 min; [M+1] = 292.16.

Step 5. Example 175

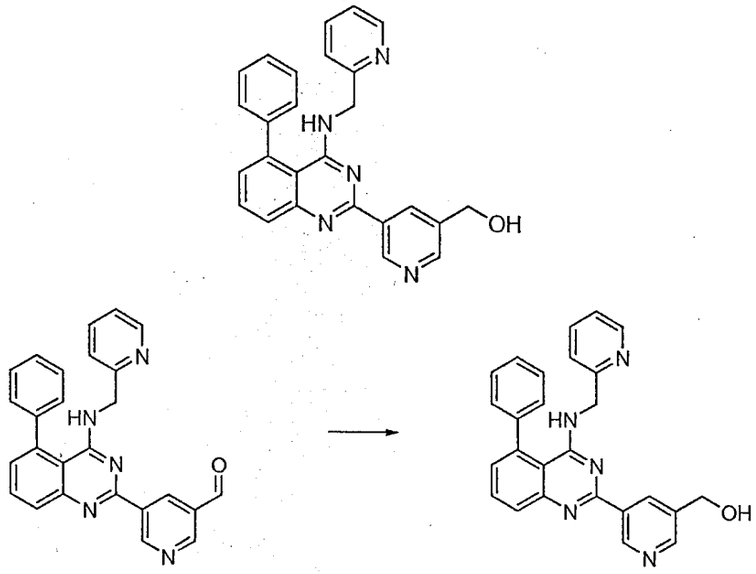


[00176] A stirred solution of 6-bromo-2-methylimidazo[1,2-a]pyridine-8-sulfonamide (0.20g, 0.68 mmol) in dioxane (10 mL) was degassed for 10min with argon and $Pd(PPh_3)_4$ (0.2 g, 0.16 mmol) and hexamethylditin (0.25 mL, 1.2 mmol) were added and the reaction mixture stirred at room temperature for 16 h. 2-Chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.58 g, 1.68 mmol) was added and the reaction mixture heated at 100 °C for an additional 16 h. A precipitate formed and the solids were filtered from the reaction mixture and the filtrate was concentrated and purified by silica gel column chromatography using

dichloromethane / methanol mixture as the eluent to get pure Example 175 (30 mg, 10 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.73 (s, 1H); 8.77 (d, 1H, J = 1.2Hz); 8.28 (d, 1H, J = 4.4Hz); 8.09 (s, 1H); 7.90 (d, 1H, J = 8.4Hz); 7.84 (t, 1H, J = 6.8Hz); 7.75 (dt, 1H, J = 6Hz, 7.6Hz); 7.61-7.50 (m, 6H); 7.43 (s, 1H); 7.36-7.25 (m, 3H); 6.85 (br s, 1H0; 4.78 (d, 2H, J = 4Hz); 2.46 (s, 3H). LCMS Method X: retention time 1.59 min; [M+1] = 522.2; HPLC Method A1: purity 98.3%, retention time = 6.63 min.

EXAMPLE 176

(5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)methanol

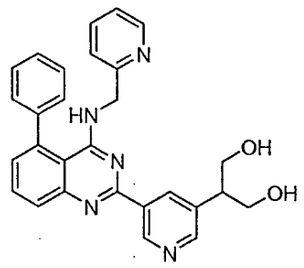


[00177] To a solution of 5-(5-phenyl-4-(pyridin-2-ylmethylamino) quinazolin-2-yl) nicotinaldehyde (described in Example 191, 1.0 g, 2.4 mmol) in ethanol (15 mL) was added $NaBH_4$ (0.28 g, 7.2 mmol). The reaction mixture was stirred at RT. A saturated solution of ammonium chloride was added and the aqueous layer was extracted with ethyl acetate. The organic layer was separated, dried, filtered and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography using a dichloromethane / methanol mixture as the eluent to provide Example 176 (0.71 g, 71 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.51 (s, 1H), 8.72 (s, 1H), 8.63 (s, 1H), 8.23 (d, 1H, J = 4.8 Hz), 7.88 (dd, 1H, J = 7.6Hz,

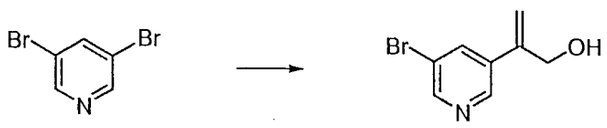
8.4Hz), 7.85 – 7.80 (m, 1H), 7.73 (dt, 1H, *J* = 1.2 Hz, 7.6Hz), 7.61-7.48 (m, 5H), 7.33 (d, 2H, *J* =19.2 Hz), 7.27 (d, 1H, *J* =14 Hz), 7.23 (dt, 1H, *J* = 1.6, 7.2 Hz), 6.87 (t, 1H, *J* = 4.0 Hz, 1H), 5.47 (t, 1H, *J*=5.6), 4.75 (d, 2H, *J*-4Hz), 4.67 (d, 2H, *J* = 5.6Hz). LCMS Method U: retention time 1.46 min; [M+1] = 420.2; HPLC Method A4: purity 99.5%, retention time = 5.77 min.

EXAMPLE 177

2-(5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)propane-1,3-diol



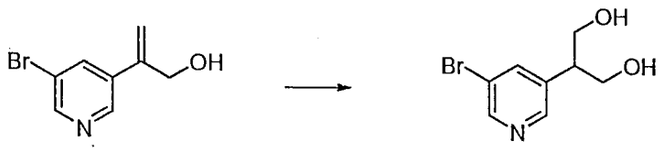
Step 1. Preparation of 2-(5-bromopyridin-3-yl)prop-2-en-1-ol.



[00178] A microwave vial was charged with 3,5-dibromo pyridine (5.00 g, 21.1 mmol), $Pd(OAc)_2$, (0.185 g, 0.820 mmol), 1,3 – Bis(diphenylphosphino)propane (0.7 g 1.7 mmol), and 1-butyl-3-methylimidazolium tetrafluoroborate (25 mL) under nitrogen at room temperature. The reaction mixture was degassed three times and allyl alcohol (2.85 g, 49.1 mmol) and triethylamine (4.7 ml, 3.6 mmol) were added. The reaction mixture was heated in microwave reactor at 125 °C for 2 h. After cooling to room temperature, aqueous HCl (20 mL, 10 %) was added and the mixture stirred for 1 h. The reaction mixture was treated with saturated Na_2CO_3 (20 mL) and the aqueous portion extracted with CH_2Cl_2. The combined organic layers were washed with water and brine, dried with Na_2SO_4 and evaporated under reduced pressure. The resulting residue was purified by flash silica gel chromatography (SiO_2,

hexane/EtOAc = 8/2) to yield 2-(5-bromopyridin-3-yl)prop-2-en-1-ol (1.6 g, 36 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.69 (d, 1H, J = 2Hz), 8.62 (d, 1H, J = 2.4Hz), 8.13 (s, 1H), 5.66 (s, 1H), 5.45 (s, 1H), 5.15 (t, 1H, J = 5.2 Hz), 4.35 (d, 2H, J = 5.2 Hz). LCMS Method T: retention time 0.96 min; [M+1] = 216.

Step 2. Preparation of 2-(5-bromopyridin-3-yl)propane-1,3-diol



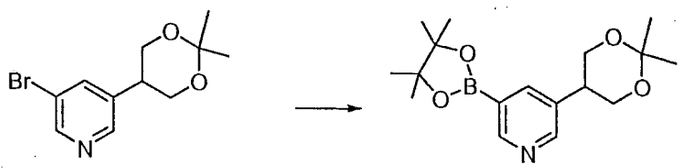
[00179] To a stirred solution of 2-(5-bromopyridin-3-yl)prop-2-en-1-ol (0.600 g, 2.79 mmol) in tetrahydrofuran (5 mL) at 0 °C under nitrogen was added borane-methyl sulfide complex (0.85 g, 11 mmol). The reaction mixture was heated to 25 °C and stirred for 5 h. The reaction mixture was cooled to 0 °C and 1.0 N sodium hydroxide (0.8 mL) was added drop wise followed by the addition of hydrogen peroxide (1.0 mL, 35 wt % solution in water). The reaction mixture was stirred at 0 °C for 2 h then partitioned between ethyl acetate and water. The aqueous layer was extracted with ethyl acetate. The organic portions were combined, washed with water, aqueous sodium sulfite and brine, dried with Na_2SO_4, filtered, and concentrated under reduced pressure. 2-(5-Bromopyridin-3-yl)propane-1,3-diol (0.29 g, 44.7 %) was isolated by silica gel column chromatography using 50 % EtOAc in hexanes as a yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.53 (d, 1H, J = 2Hz), 8.43 (d, 1H, J = 4.8Hz), 4.92 (s, 1H), 4.69 (t, 1H, J = 4.4 Hz), 3.71-3.64 (m, 2H), 3.62-3.58 (m, 2H), 2.87 (t, J = 6.4Hz). LCMS Method W: retention time 0.80 min; [M+1] = 232.

Step 3. Preparation of 3-bromo-5-(2,2-dimethyl-1,3-dioxan-5-yl)pyridine



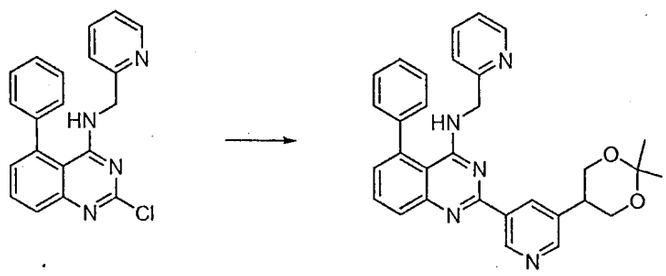
[00180] To a solution of 2-(5-bromopyridin-3-yl)propane-1,3-diol (0.12 g, 0.51 mmol) in DCM was added 2,2-dimethoxypropane (0.107 g, 1.03 mmol) and a catalytic amount of *p*-TSA. The mixture was stirred at room temperature for 3 h. The reaction mixture was quenched by the addition of sat. $NaHCO_3$ solution and the organic layer washed successively with water and brine. The organic layer was concentrated to provide the 3-bromo-5-(2,2-dimethyl-1,3-dioxan-5-yl)pyridine (0.1 g, 71.4 %), which was used without further purification. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.53 (m, 2H), 8.17 (t, 2H, J = 2Hz), 4.00-3.92 (m, 4H), 3.07-3.02 (m, 1H), 1.47 (s, 3H), 1.38 (s, 3H).

Step 4. Preparation of 3-(2,2-dimethyl-1,3-dioxan-5-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine



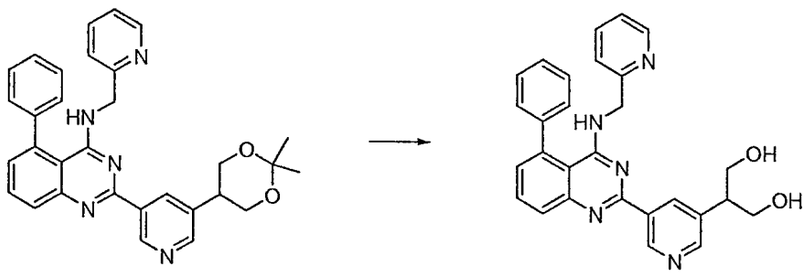
[00181] A mixture of 3-bromo-5-(2,2-dimethyl-1,3-dioxan-5-yl)pyridine (0.10 g, 0.37 mmol), bis(pinacolato)diboron (0.112 g, 0.44 mmol) and potassium acetate (0.145 g, 1.40 mmol) in 1,4-dioxane (8 mL) was degassed with nitrogen for 15 min. (1,1'-Bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (24 mg, 0.03 mmol) was added and the mixture was again degassed for 10 min. with nitrogen. The reaction mixture was heated in the microwave reactor at 120 °C for 45 min. After this time, the reaction mixture was filtered through celite and the filtrate was concentrated under reduced pressure to provide crude 3-(2,2-dimethyl-1,3-dioxan-5-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (110 mg) as a brown solid, which was used without further purification. LCMS Method W: retention time 1.46 min; [M+1] = 320.2.

Step 5. Preparation of 2-(5-(2,2-dimethyl-1,3-dioxan-5-yl)pyridin-3-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine



[00182] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl) quinazolin-4-amine (80 mg, 0.23 mmol) in 1,4-dioxane (6 mL) and H_2O (0.5 mL) under nitrogen was added 3-(2,2-dimethyl-1,3-dioxan-5-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (110 mg, 0.35 mmol), and potassium carbonate (96 mg, 7.0 mmol). The mixture was degassed with nitrogen for 15 min. (1,1'-Bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (12 mg, 0.015 mmol) was added and the reaction mixture was again degassed for 10 min with nitrogen. The reaction mixture was stirred at 90 °C for 16 h, then allowed to cool to room temperature and quenched by the addition of water. The reaction mixture was extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography using 20 % EtOAc in hexanes to provide 2-(5-(2,2-dimethyl-1,3-dioxan-5-yl)pyridin-3-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (45 mg, 39 %). LCMS Method T: retention time 1.75 min; [M+1] = 504.2.

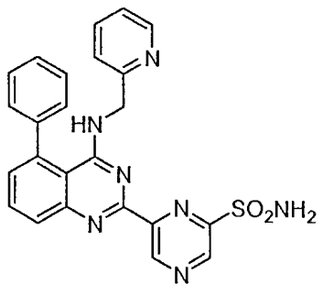
Step 6. Example 177



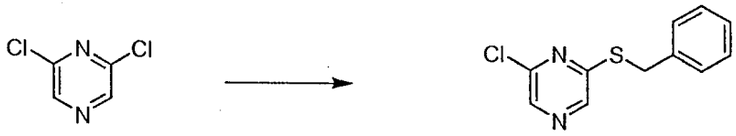
[00183] To a solution 2-(5-(2,2-dimethyl-1,3-dioxan-5-yl)pyridin-3-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (45 mg, 0.83 mmol) in methanol (5 mL) was added pTSA (30 mg, 0.17 mmol) and the mixture was stirred for 2 h. The reaction was quenched by the addition of sat. Na_2CO_3 solution and the volatile solvents removed under reduced pressure. The residue was dissolved in ethyl acetate then washed with water and brine. The organic layer was dried, concentrated and purified by filter column 80 % EtOAc in Hexanes to provide 2-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl) propane-1,3-diol (18 mg, 44 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.74 (s, 1H), 9.60 (d, 1H, J = 2Hz), 9.56 (d, 1H, J = 2Hz), 8.26 (d, 1H, J = 4.8 Hz), 7.90 (dd, 1H, J =1.2, 9.2 Hz), 7.83 (t, 1H, J = 7.2 Hz), 7.72 (dd, 1H, J = 1.8, 7.6 Hz), 7.61-7.50 (m, 5H), 7.38-7.30 (m, 2H), 7.26 (dt, 1H, J =1.2, 8 Hz), 6.80 (br s, 1H), 4.74 (d, 1H, J = 4.4 Hz), 4.70 (t, 1H, J = 5.2Hz), 3.85-3.77 (m, 2H), 3.76-3.68 (m, 2H), 3.30-2.95 (m, 1H). LCMS Method T: retention time 1.40 min; [M+1] = 464.2; HPLC Method A4: purity 99.4 %, retention time = 5.48 min.

EXAMPLE 178

6-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyrazine-2-sulfonamide



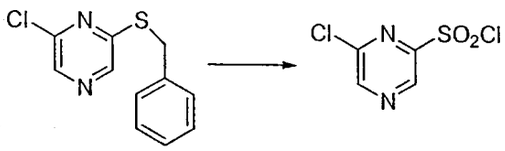
Step 1. Preparation of 2-(benzylthio)-6-chloropyrazine



[00184] To a stirred solution of 2,6-dichloropyrazine (4.50 g, 30.2 mmol) and potassium carbonate (3.75 g, 27.1 mmol) in DMF (50 mL) was added benzyl

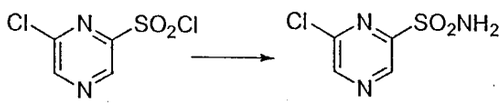
mercaptane (3.37 g, 27.1 mmol) in DMF (20 mL). The resulting mixture was stirred for 16 h at room temperature. Water (200 mL) was added to the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic portions were combined, washed successively with water, aqueous sodium sulfite and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford 2-(benzylthio)-6-chloropyrazine (6.5g, 97%) as a yellow oil, which was used without further purification. LCMS Method E: retention time 2.058 min; [M+1] = 236.6.

Step 2. Preparation of 6-chloropyrazine-2-sulfonyl chloride



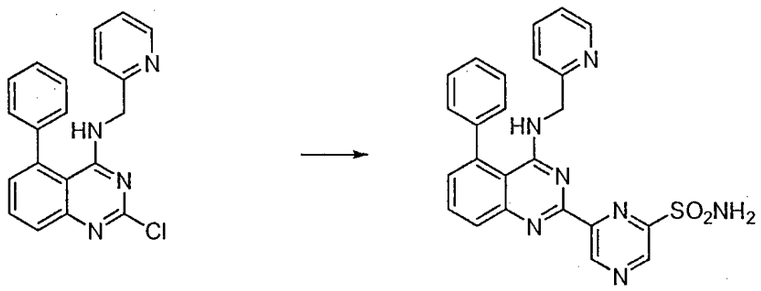
[00185] 2-(Benzylthio)-6-chloropyrazine (5.00 g, 21.2 mmol) was dissolved in carbon tetra chloride and water mixture (200ml/50ml). The reaction solution was purged with chlorine gas at 0 °C for 30 min and diluted with DCM. The organic layer was dried, filtered and concentrated under reduced pressure to yield 6-chloropyrazine-2-sulfonyl chloride as a brown oil.

Step 3. Preparation of 6-chloropyrazine-2-sulfonamide



[00186] The residue of 6-chloropyrazine-2-sulfonyl chloride from step 1 above was dissolved in THF and purged with ammonia gas at –20 °C for 15 min. The resulting mixture was stirred for 16 h at 50 °C in a sealed tube. The organic solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel using 2.5 % methanol in dichloromethane to afford 6-chloropyrazine-2-sulfonamide (1.6 g, 34 %) as white solid. LCMS Method W: retention time 0.638 min; [M+1] = 194.0.

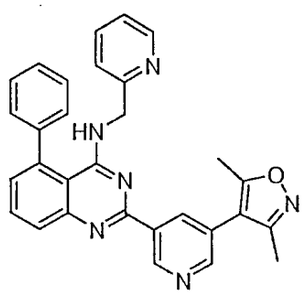
Step 4. Example 178



[00187] To a stirred solution of 6-chloropyrazine-2-sulfonamide (0.3 g, 1.56 mmol) in dioxane (10 mL) was degassed for 10 min with argon. $Pd(PPh_3)_4$ (0.17 g, 0.156 mmol) and hexamethylditin (0.48 mL, 2.3 mmol) were added and the mixture was stirred at room temperature for 16 h. 2-Chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.43 g, 1.24 mmol) and LiCl (0.16 g, 4.68 mmol) in dioxane (2 mL) were added to the reaction mixture through cannula and heated at 100 °C for an additional 16 h. The reaction mixture was concentrated under reduced pressure and water was added. The aqueous layer was extracted with ethyl acetate, and the organic extracts washed with brine, dried, filtered and concentrated under reduced pressure. The residue was purified by column chromatography using 20 % acetone in hexanes then further purified by prep HPLC (method H, Column: Waters SunFire 19 x 100 mm 5 um C18 and TFA/water, acetonitrile as the eluent) to provide 6-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyrazine-2-sulfonamide (35 mg, 9 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.84 (s, 1H),) 9.24 (s, 1H), 8.24 (d, 1H, J = 4.8Hz), 7.98-7.88 (m, 4H), 7.73 (t, 1H, J = 7.6Hz), 7.24 (t, 1H, J = 5.6Hz), 7.00 (br s, 1H), 4.77 (d, 2H, J = 3.6Hz). LCMS Method W: retention time 1.8 min; [M+1] = 469.0; HPLC Method A1: purity 98.1 %, retention time = 6.74 min.

EXAMPLE 179

2-(5-(3,5-Dimethylisoxazol-4-yl)pyridin-3-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine

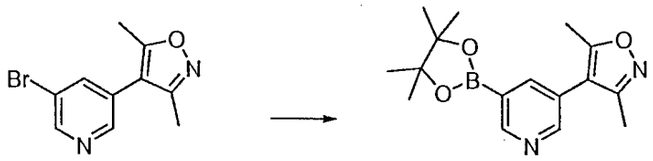


Step 1. Preparation of 4-(5-bromopyridin-3-yl)-3,5-dimethylisoxazole



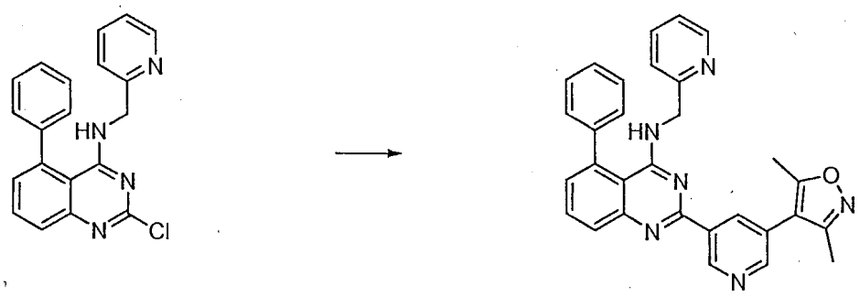
[00188] To a solution of 3,5-dibromopyridine (0.20 g, 0.85 mmol) in 1,4-dioxane (8 mL) and H_2O (0.55 mL) under nitrogen was added 3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoxazole (0.13 g, 0.93 mmol), and potassium carbonate (0.35 g, 2.5 mmol). The reaction mixture was degassed with nitrogen for 15 min. (1,1'-Bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (62 mg, 0.08 mmol) was added and the reaction mixture was again degassed for 10 min with nitrogen. The reaction mixture was stirred at 95 °C for 16 h, then allowed to cool to room temperature and quenched by the addition of water. The reaction mixture was transferred to a separation funnel and the aqueous layer extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography to provide 4-(5-bromopyridin-3-yl)-3,5-dimethylisoxazole (0.15 g, 71 %) as a white solid. LCMS Method T: retention time 1.52min, [M+1] = 253.

Step 2. Preparation of 3,5-dimethyl-4-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)isoxazole



[00189] A mixture of 4-(5-bromopyridin-3-yl)-3,5-dimethylisoxazole (0.16 g, 0.63 mmol), bis(pinacolato)diboron (0.24 g, 0.95 mmol) and potassium acetate (0.25 g, 2.4 mmol) in 1,4-dioxane (10 mL) was degassed with nitrogen for 15 min. (1,1'-Bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (0.036 g, 0.05 mmol) was added and the mixture was again degassed for 10 min. with nitrogen. The reaction mixture was heated in the microwave reactor at 120 °C for 45 min. The reaction mixture was filtered through celite and the filtrate was concentrated under reduced pressure to provide 3,5-dimethyl-4-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)isoxazole (0.17 g), which was used without further purification. LCMS Method T: retention time 0.54 min, [M+1] = 219.2.

Step 3. Example 179

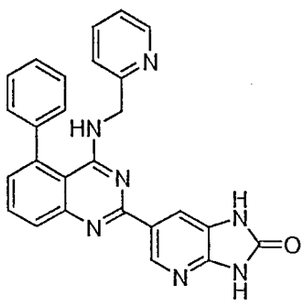


[00190] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.15 g, 0.43 mmol) in 1,4-dioxane (5 mL) and H_2O (0.55 mL) under nitrogen was added. 3,5-Dimethyl-4-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)isoxazole (0.16 g, 0.73 mmol), and potassium carbonate (0.24 g, 1.7 mmol). The reaction mixture was degassed with nitrogen for 15 min. (1,1'-Bis (diphenylphosphino) ferrocene) palladium (II) chloride dichloromethane complex (0.043 mg, 0.05 mmol) was added and the reaction mixture was again degassed for 10 min with nitrogen. The reaction mixture was stirred at 95 °C for 16 h, then allowed to cool to room temperature and quenched with water. The reaction mixture was transferred to a separation funnel and the aqueous layer extracted with ethyl acetate.

The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using dichloromethane / methanol mixture as the eluent to provide Example 179 (0.08 g, 38.2 %) as an off white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.72 (d, 1H, J = 4Hz), 8.70 (s, 1H), 8.60 (d, 1H, J = 2Hz), 8.26 (d, 1H, J = 2 Hz), 7.94 (br s, 1H), 7.74 (t, 1H, J = 7.2 Hz),7.57 (dt, 1H, J = 2Hz, 7.6 Hz), 7.52-7.48 (br s, 5H), 7.30-7.27 (m, 1H), 7.18-7.10 (m, 2H), 6.70 (br s, 1H), 4.76 (d, 2H, J = 4.0 Hz), 2.48 (s, 3H), 2.33 (s, 3H). LCMS Method T: retention time 1.82 min; [M+1] = 485.2. HPLC Method A1: purity 98.9 %, retention time = 7.67 min.

EXAMPLE 180

6-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one



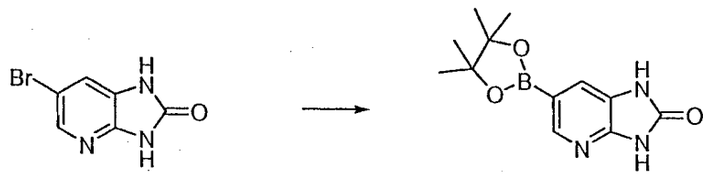
Step 1. Preparation of 6-bromo-1H-imidazo[4,5-b]pyridin-2(3H)-one



[00191] A mixture of 5-bromopyridine-2,3-diamine (2 g, 10.6 mmol) and urea (2.5 g, 41.6 mmol) was dissolved in DMF and heated to 100 °C for 16 h. The reaction mixture was diluted with water and extracted with ethyl acetate. The organic layer

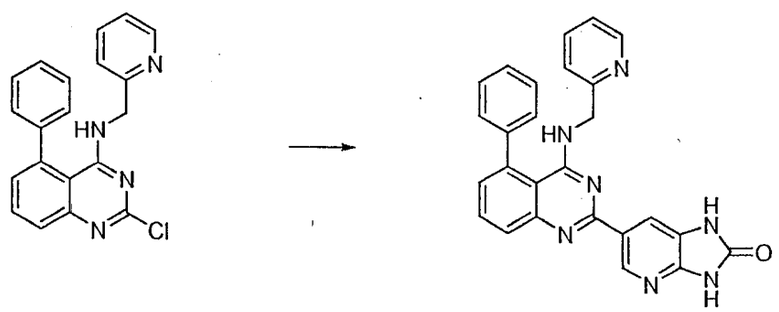
was dried over Na_2SO_4 then concentrated to provide 6-bromo-1H-imidazo[4,5-b]pyridin-2(3H)-one (0.80 g, 36 %) as an off white solid which was used without further purification. LCMS Method W: retention time 0.98 min; [M+2] = 212, 214.0.

Step 2. Preparation of 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one



[00192] A mixture of 6-bromo-1H-imidazo[4,5-b]pyridin-2(3H)-one (0.500 g, 2.35 mmol), bis(pinacolato)diboron (0.895 g, 3.53 mmol) and potassium acetate (0.924 g, 9.42 mmol) in 1,4-dioxane (10 mL) was degassed with nitrogen for 15 min. (1,1'-Bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (0.192 g, 0.23 mmol) was added and the reaction mixture was again degassed for 10 min. with nitrogen. The reaction mixture was heated in the microwave reactor at 120 °C for 45 min. The reaction mixture was filtered through celite and the filtrate was concentrated under reduced pressure to provide 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one (0.3 g, 49 %) which was used without further purification. LCMS Method Y: retention time 1.5 min; [M+1] = 261.7.

Step 3. Example 180

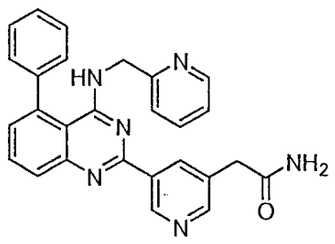


[00193] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.25 g, 0.72 mmol) in 1,4-dioxane (10 mL) and H_2O (2 mL) under nitrogen was added. 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-imidazo[4,5-

b]pyridin-2(3H)-one (0.28 g, 1.1 mmol) and potassium carbonate (0.2 g, 1 mmol). The mixture was degassed with nitrogen for 15 min. (1,1'-bis(diphenylphosphino)-ferrocene)palladium (II) chloride dichloromethane complex (0.06 mg, 0.07 mmol) was added and the reaction mixture was again degassed for 10 min with nitrogen. The reaction mixture was stirred at 90 °C for 16 h, then allowed to cool to room temperature and quenched with water. The reaction mixture was transferred to a separation funnel and the aqueous layer extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using dichloromethane/methanol mixture as the eluent to provide Example 180 (0.038 g, 12 % yield) as brown solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 11.14 (br, 1H), 9.06 (s, 1H), 8.25(d, 1H, J = 4.4 Hz), 8.20 (s, 1H), 7.86-7.77 (m, 2H), 7.72 (t, 1H, J = 8 Hz), 7.60-7.49 (m, 5H), 7.31 (d, 1H, J =1.2 Hz), 7.26-7.20 (m, 2H), 6.75 (br s, 1H), 4.72 (d, 1H, J = 4.0 Hz). LCMS Method T: retention time 1.56 min; [M+1] = 446.2.0. HPLC Method A1: purity 99.09 %, retention time = 5.83 min.

EXAMPLE 181

2-(5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)acetonitrile



Step 1. Preparation of 3-bromo-5-chloromethyl-pyridine



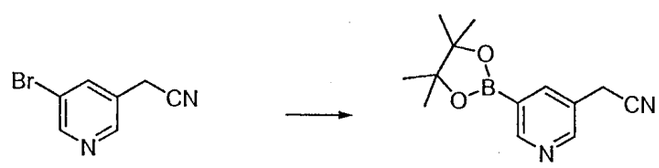
[00194] To a solution of (5-bromo-pyridin-3-yl)-methanol, (0.500 g, 2.68 mmol) in DCM (10 mL) was added thionyl chloride (0.5 mL) and the resulting solution was stirred at room temperature for 2 h. The reaction mixture was quenched by the addition of water and extracted into DCM. The organic extracts were washed with brine filtered and concentrated under reduced pressure to provide 3-bromo-5-chloromethyl-pyridine (0.45 g, 82 %), which was used without further purification.

Step 2. Preparation of 2-(5-bromopyridin-3-yl) acetonitrile



[00195] 3-Bromo-5-chloromethyl-pyridine (0.45 g; 2.2 mmol) was dissolved in DMF (10 mL). Potassium cyanide (0.21 g, 3.27 mmol) was added and the reaction mixture was stirred at room temperature for 16 h. The reaction mixture was quenched by the addition of water and extracted with ethyl acetate. The organic phases were washed with water, brine and dried over Na_2SO_3 filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using 7 % EtOAc in Hexanes to provide 2-(5-bromopyridin-3-yl) acetonitrile (200 mg, 46.5 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.68 (d, 1H, J = 2Hz), 8.51 (d, 1H, J = 2Hz), 7.88 (t, 1H, J = 2Hz), 3.77 (s, 2H).

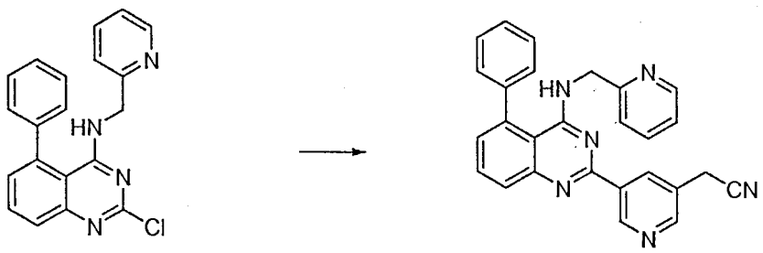
Step 3. Preparation of 2-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)acetonitrile



[00196] A mixture of 2-(5-bromopyridin-3-yl)acetonitrile (1.5 g, 7.6 mmol), bis (pinacolato)diboron (2.9 g, 12 mmol) and potassium acetate (2.98 g, 30.0 mmol) in 1,4-dioxane (15 mL) was degassed with nitrogen for 15 min. (1,1'-Bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (450 mg, 0.61 mmol) was added and the reaction mixture was again degassed for 10

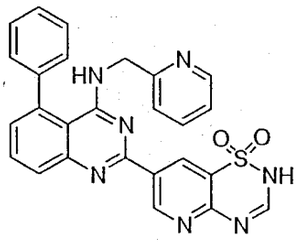
min. with nitrogen. The reaction mixture was heated in the microwave reactor at 95 °C for 16 h. The reaction mixture was filtered through celite and the filtrate was concentrated under reduced pressure to provide 2-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)acetonitrile (1.6 g) as brown solid, which was used without further purification. LCMS Method W: retention time 1.34 min; [M+1] = 245.2.

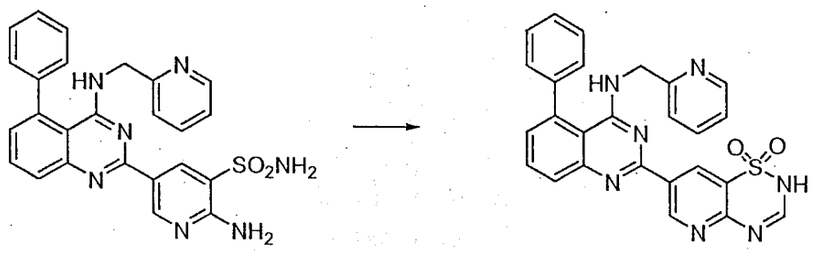
Step 4. Example 181



[00197] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl) quinazolin-4-amine (180 mg, 0.52 mmol) in 1,4-dioxane (6 mL) and H_2O (0.5 mL) under nitrogen was added. 2-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)acetonitrile (190 mg, 0.77 mmol), and potassium carbonate (215 mg, 1.55 mmol). The mixture was degassed with nitrogen for 15 min. (1,1'-bis(diphenylphosphino)-ferrocene)palladium (II) chloride dichloromethane complex (38 mg, 0.52 mmol) was added and the reaction mixture was again degassed for 10 min with nitrogen. The reaction mixture was stirred at 95 °C for 16 h, then allowed to cool to room temperature and quenched with water. The reaction mixture was transferred to a separation funnel and the aqueous layer extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using 5% methanol in dichloromethane as the eluent to provide Example 181 (110 mg, 49.6 %) as off white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.60 (s, 1H); 8.80 (s, 1H0; 8.70 (s, 1H); 8.24 (d, 1H, J = 4.8 Hz); 7.90 (dd, 1H, J = 1.6, 8.4Hz); 7.84 (t, 1H, J = 7.2Hz); 7.73 (dt, 1H, J = 1.6, 7.6Hz); 7.62-7.50 (m, 5H); 7.36-7.30 (m, 2H); 7.23 (dd, 1H, J = 1.6, 7.2Hz); 6.89 (t, 1H, J = 4Hz); 4.75 (d, 2H, J = 4Hz); 4.27 (s, 2H). LCMS Method Y: retention time 1.94 min; [M-1] = 427.0; HPLC Method A1: purity 99.4 %, retention time = 6.95 min.

EXAMPLE 182

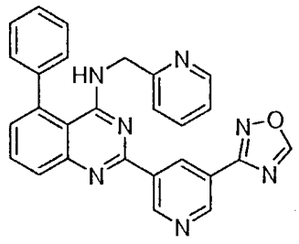




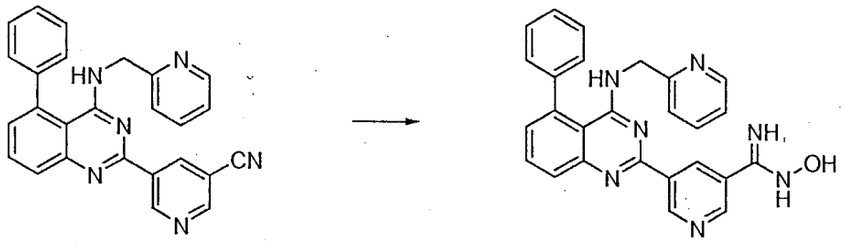
[00198] 2-Amino-5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridine-3-sulfonamide (Example 168, 0.095 g, 0.19 mmol) was dissolved in trimethylorthoformate (10 mL) and refluxed at 110 °C for 16 h. The volatile solvents were evaporated under reduced pressure and the residue was purified by silica gel column chromatography using 30 % acetone in hexanes mixture as the eluent to provide Example 182 (4 mg, 4 %) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 13.10 (br s, 1H); 9.71 (d, 1H, J = 2Hz); 9.11 (d, 1H, J = 2Hz); 8.24 (d, 1H, J = 4.4Hz); 8.12 (s, 1H); 7.93 (d, 1H, J = 8.4Hz); 7.85 (t, 1H, J = 8Hz); 7.73 (dt, 1H, J 1.2, 8Hz); 7.61-7.49 (m, 5H); 7.33 (dd, 2H, J = 8, 10.8Hz); 7.23 (t, 1H, J = 8Hz); 6.96 (br t, 1H, J = 4Hz);4.75 (d, 2H, J = 8Hz). LCMS Method W: retention time 1.91 min; [M+1] = 494.2; HPLC Method A4: purity 98.0 %, retention time = 7.65 min.

EXAMPLE 183

2-(5-(1,2,4-Oxadiazol-3-yl)pyridin-3-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine

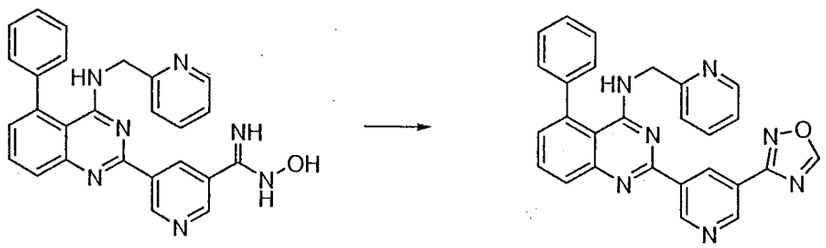


Step 1. Preparation of N-hydroxy-5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinimidamide



[00199] To a solution of ethyl 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinonitrile (described in Example 6, 0.10 g, 0.24 mmol) in ethanol (5 mL) was added hydroxylamine hydrochloride (0.033 g, 0.48 mmol) and potassium carbonate (0.076 g, 0.72 mmol). The reaction mixture was heated to reflux at 80 °C for 16 h. The ethanol solvent was evaporated under reduced pressure and the residue was dissolved in DCM, and washed with water. The organic layer was dried, filtered and concentrated to provide N-hydroxy-5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinimidamide (0.2 g) which was used without further purification. LCMS Method X: retention time 1.788 min; [M+1] = 448.0.

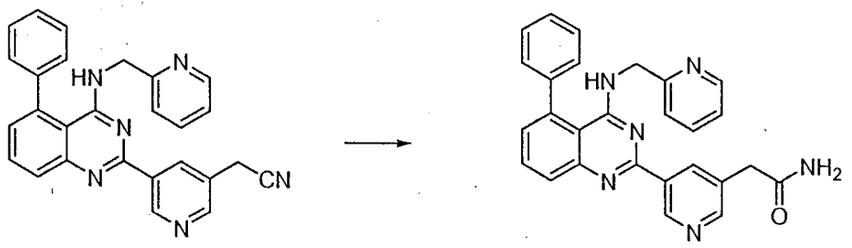
Step 2. Example 183



[00200] N-hydroxy-5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinimidamide (0.10 g, 0.22 mmol) was dissolved in trimethylorthoformate (5 mL) and pTSA (cat.) was added. The reaction mixture was refluxed at 100 °C for 16 h. The volatile solvents were evaporated under reduced pressure and the residue was purified by silica gel column chromatography 1.6 % methanol in DCM to provide Example 183 (4 mg, 4 % yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.83 (s, 1H), 9.37-9.31 (m, 2H); 8.25 (d, 1H, J = 4Hz); 7.96 (dd, 1H, J = 1.2, 8.4Hz); 7.87 (dd, 1H, J = 6.8, 8.4Hz); 7.73 (dd, 1H, J = 1.6, 7.6Hz): 7.62-7.50 (m, 5H); 7.40-7.33 (m, 2H); 7.24 (dd, 1H, J, = 4.8, 6.8Hz); 6.94 (br s, 1H); 4.77 (d, 2H, J = 4.4Hz). LCMS Method Y: retention time 2.03 min; [M+1] = 458.2; HPLC Method A4: purity 94.7 %, retention time = 7.4 min.

EXAMPLE 184

2-(5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)acetamide

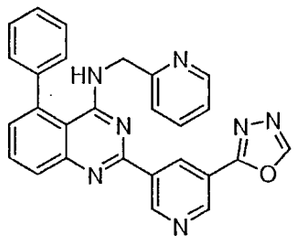


[00201] To a solution of 2-(5-(5-phenyl-4-(pyridin-2-ylmethylamino) quinazolin-2-yl)pyridin-3-yl) acetonitrile (Example 181) (70 mg, 20.1 mmol) in ethanol/H_2O (3/3 mL) was added sodium hydroxide (40 mg, 1.0 mmol) The mixture was heated under reflux for 2 h. The reaction mixture was quenched by the addition of water (5 mL) and extracted with ethyl acetate. The organic extracts were washed with saturated brine and dried over anhydrous magnesium sulfate and filtered. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography (silica gel. MeOH/DCM, 2.5:97.5) to provide Example 184 (32 mg, 44 %) as an off white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.50 (s, 1H); 8.68 (s, 1H); 8.59 (s, 1H); 8.25 (d, 1H, J = 4.4Hz); 7.89 (dd, 1H, J = 1.2, 7.6Hz); 7.83 (t, 1H, J = 7.2Hz); 7.73 (dt, 1H, J = 1.6, 7.6 Hz); 7.65 (br s, 1H); 7.60-7.50 (m, 5H); 7.38-7.30 (m, 2H); 7.23 (t, 1H, J = 6.4Hz); 7.22 (br s, 1H); 6.84 (br s, 1H); 4.75 (d,

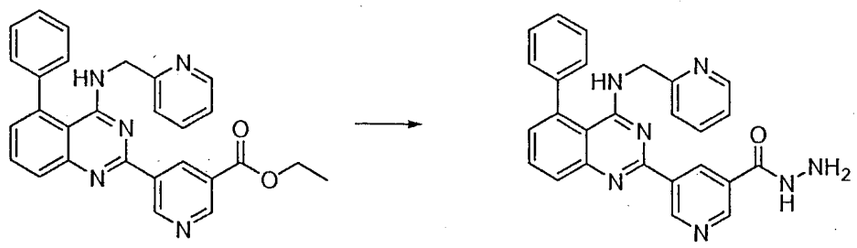
2H, *J* = 4Hz); 3.57 (s, 2H). LCMS Method Y: retention time 1.72 min; [M+1] = 447.2; HPLC Method A4: purity 97.8 %, retention time = 5.48 min.

EXAMPLE 185

2-(5-(1,3,4-Oxadiazol-2-yl)pyridin-3-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine

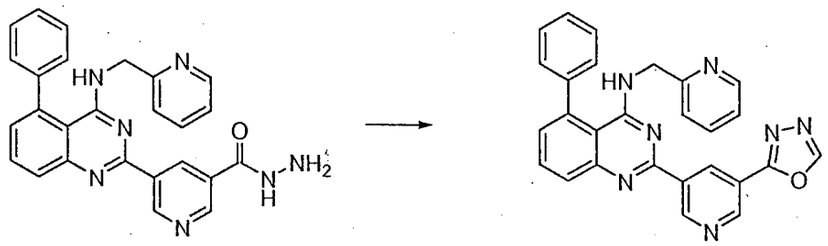


Step 1. Preparation of 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinohydrazide



[00202] To a solution of ethyl 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinate (Example 43) (0.2 g, 0.43 mmol) in ethanol (10 mL) was added hydrazine hydrate (0.1 mL, 2.1 mmol). The reaction mixture was heated to reflux at 80 °C for 16 h. The ethanol was evaporated under reduced pressure and the residue was dissolved in DCM and washed with water. The organic layer was dried and concentrated to provide 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinohydrazide (0.2 g, crude), which was used without further purification. LCMS Method E: retention time 1.8 min; [M+1] = 447.50.

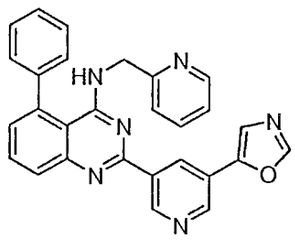
Step 2. Example 185



[00203] 5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinohydrazide (0.2 g, 0.44 mmol) was dissolved in trimethylorthoformate (5 mL). pTSA (catalytic) was added and the reaction mixture was heated to reflux at 110 °C for 16 h. The volatile solvents were evaporated under reduced pressure and the residue was purified by silica gel column chromatography 1.7 % methanol in DCM to provide Example 185 (4 mg, 2 %) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.86 (s, 1H), 9.53 (s, 1H); 9.33 (s, 1H); 9.31 (s, 1H); 8.25 (br s, 1H); 7.96 (dd, 1H, J = 1.2, 1.8Hz); 7.87 (dd, 1H, J = 7.2, 8Hz); 7.74 (dt, 1H, J = 1.8Hz); 7.62-7.50 (m, 5H); 7.34 (dd, 2H, J = 7.2, 12.8Hz); 7.25 (dd, 1H, J = 4.8, 6.4Hz); 6.95 (t, 1H, J = 4Hz); 4.77 (d, 2H, J = 4.4Hz). LCMS Method Y: retention time 1.91 min; [M+1] = 458.2; HPLC Method A1: purity 96.7 %, retention time = 6.85 min.

EXAMPLE 186

2-(5-(Oxazol-5-yl)pyridin-3-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine

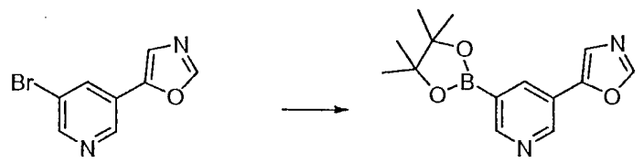


Step 1. Preparation of 5-(5-bromopyridin-3-yl)oxazole



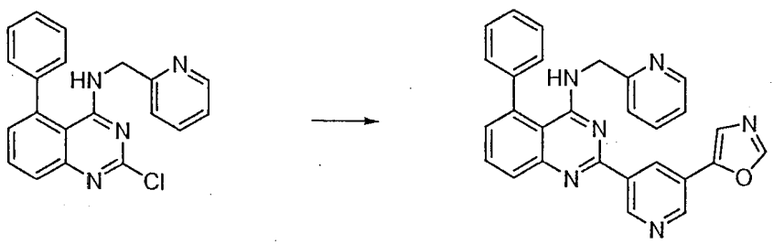
[00204] To a solution of 5-bromonicotinaldehyde (0.2 g, 1 mmol) in MeOH (5 mL) was added K_2CO_3 (0.3 g, 2 mmol) followed by TOSMIC (0.27 g, 1.39 mmol). The mixture was heated to 85 °C for 2 h. Methanol was evaporated under reduced pressure and the residue was dissolved in DCM then washed with water. The organic extracts were dried over sodium sulfate, filtered and concentrated. The residue was purified by silica gel column chromatography using 2.1 % MeOH in DCM as the eluent to provide 5-(5-bromopyridin-3-yl)oxazole (0.12 g. 50 %). LCMS Method Y: retention time 1.39 min; [M+1] = 225.0.

Step 2. Preparation of 5-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)oxazole



[00205] A mixture of 5-(5-bromopyridin-3-yl)oxazole (0.10 g, 0.044 mmol), bis(pinacolato)diboron (0.17 g, 0.60 mmol) and potassium acetate (0.129 g, 1.3 mmol) in 1,4-dioxane (5 mL) was degassed with nitrogen for 15 min. (1,1'-Bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (0.017 g, 0.022 mmol) was added and the mixture was again degassed for 10 min. with nitrogen. The reaction mixture was heated in the microwave at 100 °C for 16 h. The reaction mixture was filtered through celite and the filtrate was concentrated under reduced pressure to provide 5-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)oxazole (0.1 g), which was used without further purification. LCMS Method W: retention time 1.45 min; [M+1] = 273.2.

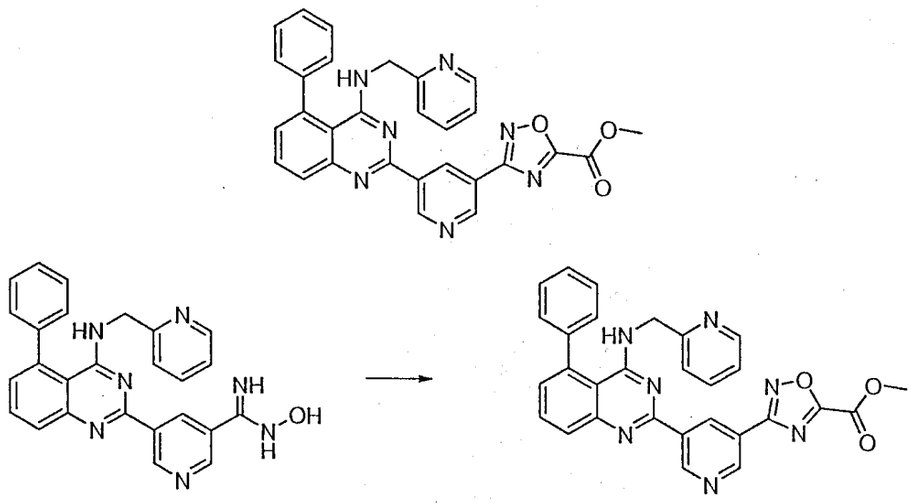
Step 3. Example 186



[00206] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.115 g, 0.330 mmol) in 1,4-dioxane (6 mL) and H_2O (1.5 mL) under nitrogen was added, 5-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)oxazole (0.10 g, 0.36 mmol) and potassium carbonate (0.136 g, 0.990 mmol). The reaction mixture was degassed with nitrogen for 15 min. (1,1'-Bis(diphenylphosphino)-ferrocene)palladium (II) chloride dichloromethane complex (0.026 g, 0.033 mmol) was added and the reaction mixture was again degassed for 10 min with nitrogen. The reaction mixture was stirred at 100 °C for 16 h, then allowed to cool to room temperature and quenched with water. The reaction mixture was transferred to a separation funnel and the aqueous layer extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using 5 % methanol in dichloromethane to provide 2-(5-(oxazol-5-yl)pyridin-3-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.015 g) as a brown solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.70 (s, 1H); 9.03 (s, 1H); 8.27 (d, 2H, J = 3.6Hz); 8.03 (s, 1H0; 7.77 (t, 1H, J = 7.6Hz); 7.70-7.58 (m, 2H); 7.54-7.47 (m, 5H0; 7.33-7.28 (m, 1H); 7.20-7.10 (m, 5H0; 6.82 (br, 1h); 4.80 (d, 2H, J = 4.4Hz). LCMS Method Y: retention time 1.98 min; [M+1] = 457.2; HPLC Method A1: purity 98.7 %, retention time = 7.09 min.

EXAMPLE 187

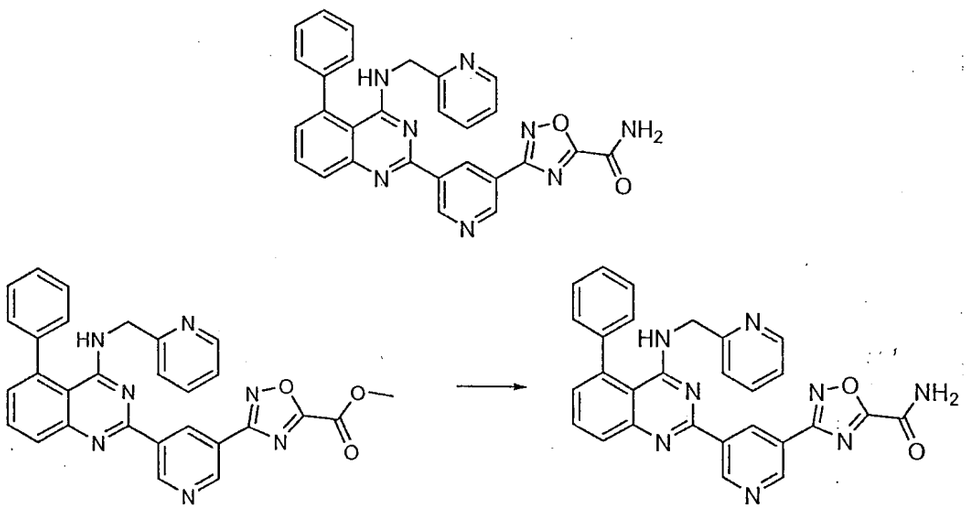
Methyl 3-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)-1,2,4-oxadiazole-5-carboxylate



[00207] To a solution of N-hydroxy-5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinimidamide (described in Example 183, 1.0 g, 2.2 mmol) in DCE at 0 °C was added methyl 2-chloro-2-oxoacetate (0.31 mL, 3.3 mmol). The reaction mixture was stirred at room temperature for 2 h. Phosphorus oxychloride (1 mL) was added and the reaction mixture was heated to reflux for 1.5 h. The reaction mixture was quenched by the addition of saturated solution of $NaHCO_3$ and extracted with DCM, dried over sodium sulfate and concentrated. The residue was purified by silica gel column chromatography using 5 % methanol in dichloromethane to provide Example 187 (270 mg, 23 %) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.85 (s, 1H); 9.34 (s, 1H0; 8.27 (d, 1H, J = 5.2Hz); 7.98 (dd, 1H, J 1.2, 8Hz); 7.87 (t, 1H, J = 4.8Hz); 7.76 (t, 1H, J = 3Hz); 7.63-7.53 (m, 5H0; 7.41-7.30 (m, 2H0; 7.24 (t, 1H, J = 6Hz); 6.95 (br s, 1H); 4.77 (d, 2H, J = 4Hz); 4.05 (s, 3H). LCMS Method Y: retention time 2.09 min; [M+1] = 516.2; HPLC Method A4: purity 97.4 %, retention time = 8.77 min.

EXAMPLE 188

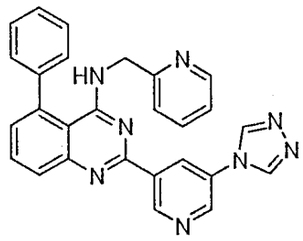
3-(5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)-1,2,4-oxadiazole-5-carboxamide



[00208] To a solution of methyl 3-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)-1,2,4-oxadiazole-5-carboxylate (Example 187, 0.080 g, 0.15 mmol) was added ammonia in methanol (10 mL) and the reaction mixture was heated at 60 °C for 4 h. The solvent was evaporated under reduced pressure to provide Example 188 (0.032 g, 45 %) as white solid. ^{1}H NMR (400 MHz, DMSO-d6, δ): 9.84 (s, 1H); 9.36 (s, 1H0; 9.34 (s, 1H); 8.80 (br s, 1H); 8.35 (br s, 1H); 8.26 (d, 1H, J = 4.8Hz); 7.98 (d, 1H, J = 8.4Hz); 7.87 (t, 1H, J = 8Hz); 7.74 (t, 1H, J 8Hz); 7.63-7.50 (m, 3H); 7.41-7.33 (m, 2H); 7.25 (t, 1H, J = 7.2Hz); 6.96 (br t, 1H, J = 4Hz); 4.78 (d, 2H, J = 4Hz). LCMS Method Y: retention time 1.89min, [M+1] = 501.2; HPLC Method A1: purity 96.4 %, retention time = 7.05 min.

EXAMPLE 189

2-(5-(4H-1,2,4-triazol-4-yl)pyridin-3-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine

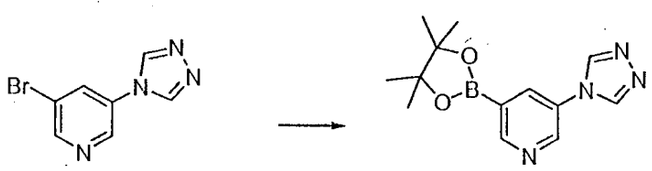


Step 1. Preparation of 3-bromo-5-(4H-1,2,4-triazol-4-yl)pyridine



[00209] A mixture of 3-bromo-5-amino pyridine (0.30 g, 1.7 mmol) and N,N-diformaylhydrazine (0.15 g, 1.7 mmol) was heated at 150 °C in sealed tube for 16 h. A precipitate formed which was dissolved in hot ethanol and then filtered. Diethyl ether was added to the filtrate at room temperature and the slurry was stirred overnight. The resulting solid was separated and purified by silica gel column chromatography using ethyl acetate and hexanes mixture as the eluent to provide 3-bromo-5-(4H-1,2,4-triazol-4-yl)pyridine (130 mg, 33 % yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.24 (s, 2H); 9.03 (d, 1H, J = 2Hz); 8.79 (d, 1H, J = 2Hz); 8.60 (t, 1H, J = 2Hz).

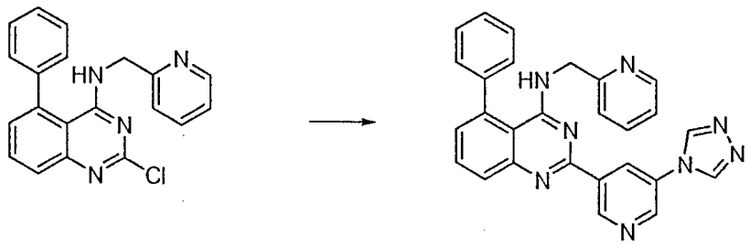
Step 2. Preparation of 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(4H-1,2,4-triazol-4-yl)pyridine



[00210] A mixture of 3-bromo-5-(4H-1,2,4-triazol-4-yl)pyridine (0.12 g, 0.50 mmol), bis(pinacolato)diboron (0.16 g, 0.60 mmol) and potassium acetate (0.15 g, 1.5 mmol) in 1,4-dioxane (10 mL) was degassed with nitrogen for 15 min. (1,1'-

Bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (0.043 g, 0.05 mmol) was added and the resulting mixture was again degassed for 10 min. with nitrogen. The reaction mixture was heated in the microwave reactor at 120 °C for 45 min. After this time, the reaction mixture was filtered through celite and the filtrate was concentrated under reduced pressure to provide 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(4H-1,2,4-triazol-4-yl)pyridine (150 mg), which was used without further purification.

Step 3. Example 189

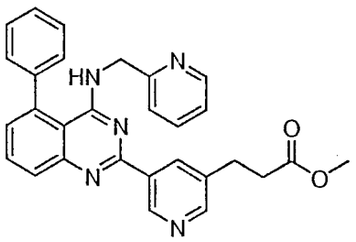


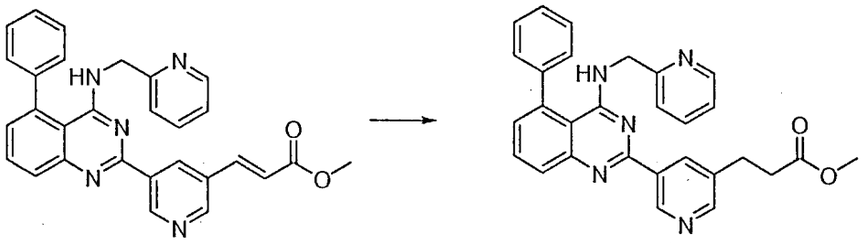
[00211] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (180 mg, 0.5 mmol) in 1,4-dioxane (6 mL) and H_2O (1 mL) under nitrogen was added 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(4H-1,2,4-triazol-4-yl)pyridine (150 mg, 0.700 mmol) and potassium carbonate (215 mg, 1.50 mmol). Upon completion of addition, the mixture was degassed with nitrogen for 15 min and then. (1,1'-bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (0.041 g, 0.050 mmol) was added. The reaction mixture was again degassed for 10 min with nitrogen. At the conclusion of this period, the reaction mixture was stirred at 90 °C for 16 h, allowed to cool to room temperature and then quenched with water. The reaction mixture was transferred to a separation funnel and the aqueous layer was extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by preparative TLC using 5% methanol in dichloromethane to afford Example 189 (6 mg, 3 % yield) as a brown solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.70 (s, 1H), 9.34 (s, 2H), 9.07 (s, 1H), 8.97 (s, 1H), 8.22 (d, 1H, J = 4.4 Hz), 7.93 (dd, 1H, J = 1.2, 8.4 Hz), 7.86 (t, 1H, J = 6 Hz), 7.73 (dt, 1H, J = 1.6, 7.6 Hz), 7.50-7.62 (m, 5H); 7.36-7.32 (m, 2H); 7.23

(t, 1H, J = 5.6 Hz), 6.97 (t, 1H, J = 4 Hz), 4.79 (d, 2H, J = 4.0 Hz). LCMS Method Y: retention time 1.79 min; [M-1] = 455.2; HPLC Method A3: purity 98.9 %, retention time = 13.5min.

EXAMPLE 190

Methyl 3-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)propanoate



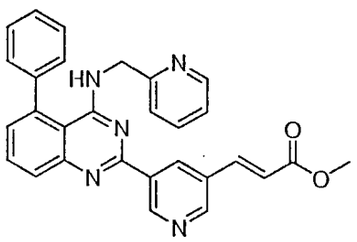


[00212] To a solution of (E)-methyl 3-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)acrylate (Example 191, prepared in a similar manner to the procedure described below, 0.3 g, 6.3 mmol) in ethanol (7 mL) was added 10 % palladium-on-carbon (100 mg). Upon completion of addition, the reaction mixture was stirred at RT under hydrogen for 16 h. After this time, the reaction mixture was filtered through celite, and the solvent was evaporated under reduced pressure. The resulting residue was purified by silica gel column chromatography using methanol in DCM (2:98) as the eluent to provide Example 190 (180 mg, 60 % yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.47 (s, 1H), 8.63-8.57 (m, 2H), 8.23 (br s, 1H), 7.87 (d, 1H, J = 6.8 Hz), 7.82 (t, 1H, J = 6.8 Hz), 7.72 (dt, 1H, J = 2, 7.6 Hz), 7.63 -7.49 (m, 5H), 7.36 -7.28 (m, 2H), 7.23 (dd, 1H, J =5.2, 6.8Hz), 6.83 (t, 1H, J = 4.4 Hz), 4.73 (d, 2H, J = 2 Hz), 3.00 (t, 2H, J = 7.6 Hz), 2.76

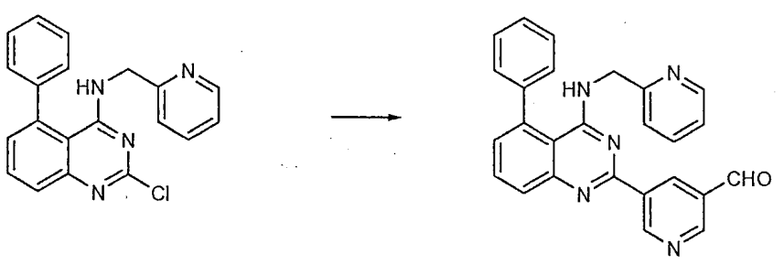
(t, 2H, J = 7.6Hz). LCMS Method W: retention time 2.17 min; [M+1] = 476.2; HPLC Method A1: purity 98.7 %, retention time = 7.10 min.

EXAMPLE 191

(E)-methyl 3-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)acrylate



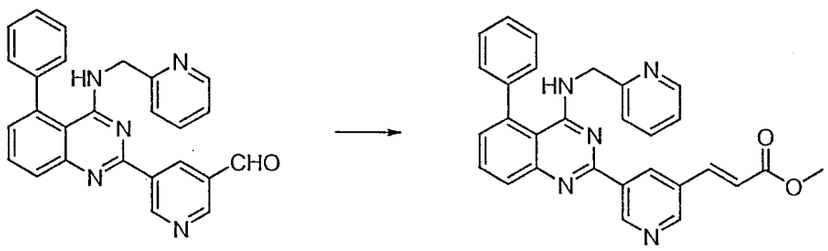
Step 1. Preparation of 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinaldehyde



[00213] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (2g, 5.7mmol) in 1,4-dioxane (40mL) and H_2O (8mL) under nitrogen was added 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)nicotinaldehyde (1.48 g, 6.30 mmol), and potassium carbonate (2.39 g, 17.0 mmol). Upon completion of addition, the reaction mixture was degassed with nitrogen for 15 min and then (1,1'-bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (0.46 mg, 0.050 mmol) was added. The reaction mixture was again degassed for 10 min with nitrogen. At the conclusion of this period, the reaction mixture was stirred at 90 °C for 16 h, then allowed to cool to room temperature and quenched by the addition of water. The reaction mixture was transferred to a separation funnel and the aqueous layer was extracted with ethyl acetate. The combined organic portions were

washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting concentrate was purified by silica gel column chromatography using 2.7 % MeOH in DCM as eluent to afford 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinaldehyde (1.8 g, 100 % yield) as an off-white solid. LCMS Method Y: retention time 1.99 min; [M+1] = 418.4.

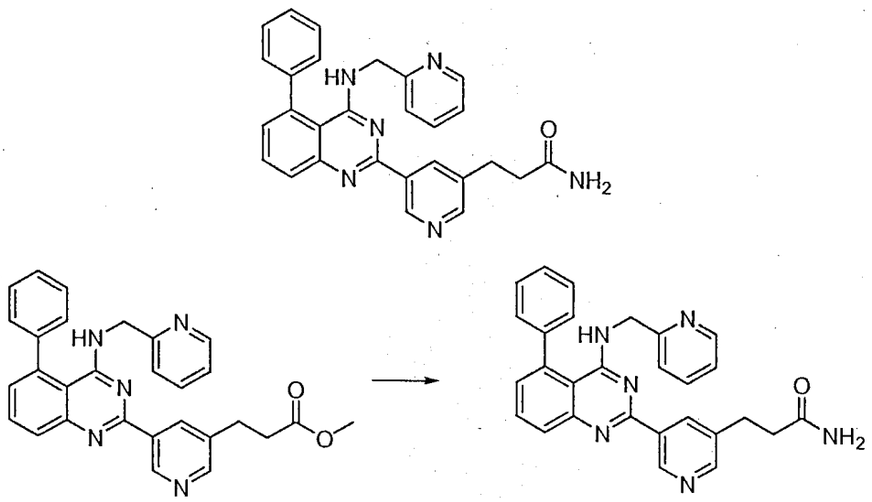
Step 2. Example 191



[00214] To a solution of 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinaldehyde (250 mg, 0.60 mmol) in THF (15 mL) was added methyl (triphenylphosphoranylidine)acetate (300 mg, 0.9 mmol). The resulting solution was stirred at room temperature for 16 h. After this time, the solvent was removed under reduced pressure to yield a residue. The residue was purified by silica gel column chromatography using 20 % EtOAc, hexane as the eluent to provide Example 191 (0.18 g, 63 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.57 (s, 1H), 8.31 (d, J=4.8, 1H), 8.15 (d, J=8.4Hz, 1H), 8.04-7.89 (m, 1H), 7.92-7.84 (m, 2H), 7.63-7.55 (m, 5H),7.51-7.43 (m, 2H), 7.37 (t, J=5.6Hz, 1H), 7.00 (d, J=16 Hz, 1H), 4.93 (d, J=4 Hz, 2H), 3.79 (s, 3H). LCMS Method Y: retention time 2.15 min; [M+1] = 474.1; HPLC Method A1: purity 99.0 %, retention time = 7.85min.

EXAMPLE 192

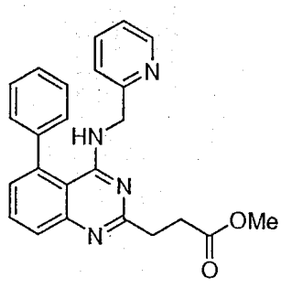
3-(5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)propanamide



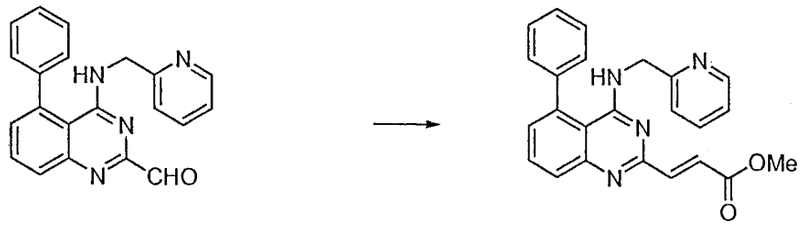
[00215] A solution of Example 190 (0.1 g, 0.2 mmol) in NH_3 (2.0 M in MeOH, 5 mL) was stirred at room temperature in a sealed vessel for 30 min. After this time, the solid formed was collected by filtration and washed with ice cooled methanol. The solid was further purified by silica gel column chromatography using 5 % methanol in DCM as the eluent to provide Example 192 (35 mg, 35 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.45 (s, 1H); 8.55 (s, 1H); 8.24 (d, 1H, J = 4Hz); 7.88 (dd, 1H, J = 1.2, 8.0Hz): 7.80 (t, 1H< J = 8Hz); 7.72 (dt, 1H, J =1.2, 8Hz); 7.60-749 (m, 5H); 7.40-7.30 (m, 2H); 7.29 (dd, 1H, J = 1.2, 7.2Hz); 7.23 (dd, 1H, J = 5.2, 6.8Hz); 6.84 (t, 1H, 3.2Hz); 4.73 (d, 2H, 4Hz); 2.95 (t, 2H, J = 7.6Hz); 2.48 (t, 2H, 7.6Hz). LCMS Method W: retention time 1.64 min; [M+1] = 461.2; HPLC Method A1: purity 99.1 %, retention time = 5.76 min.

EXAMPLE 193

Methyl 3-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)propanoate

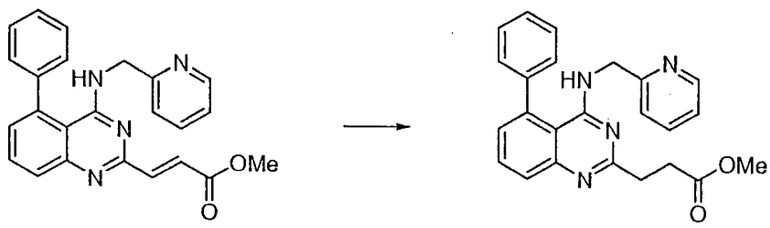


Step 1. Preparation of (E)-methyl 3-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl) acrylate



[00216] A solution of trimethyl phosphonoacetate (0.225 g 1.00 mmol) in THF (20 mL) was added 95 % sodium hydride (0.050 g, 2.0 mmol). Upon the completion of addition, the mixture was stirred at 0 °C for 30 min and then 5-phenyl-4-(pyridin-2-ylmethylamino)quinazoline-2-carbaldehyde (Example 212, prepared in a similar manner to the procedure described below, 0.340 g, 1.00 mmol) was added to the reaction mixture. The resulting mixture was stirred at room temperature for 14 h. After this time, the reaction mixture was quenched with saturated aqueous ammonium chloride solution (50 mL) and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and filtrated. The filtrate was concentrated and the resulting residue was subjected to silica gel column chromatography using 5% MeOH in chloroform as the eluent to provide (E)-methyl 3-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl) acrylate (0.30 g, 72 %) as a brown solid. LCMS Method V: retention time 1.94 min; [M+1] = 411.2.

Step 2. Example 193

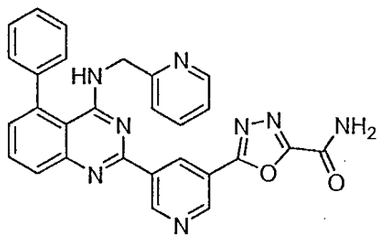


[00217] To a solution of (E)-ethyl 3-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl) acrylate (0.150 g, 0.370 mmol) in MeOH (25 mL) was added 10 % palladium-on-carbon (50 mg). The mixture is stirred at room temperature under hydrogen for 14 h. After this time, the mixture was filtered to provide Example 193 (110 mg, 73 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.21

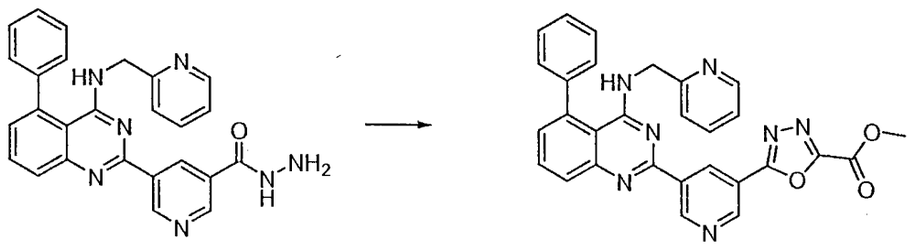
(d, 1H, J = 4.4Hz); 7.76-7.66 (m, 3H); 7.55-7.45 (m, 5H); 7.24-7.19 (m, 3H); 6.65 (br s, 1H); 4.54 (d, 2H, J = 4.4Hz); 3.60 (s, 3H0; 3.06 (t, 2H, J = 6Hz); 2.82 (t, 2H, J = 6Hz). LCMS Method Y: retention time 1.87 min; [M+1] = 399.4; HPLC Method A1: purity 94.0 %, retention time = 6.32 min.

EXAMPLE 194

5-(5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)-1,3,4-oxadiazole-2-carboxamide



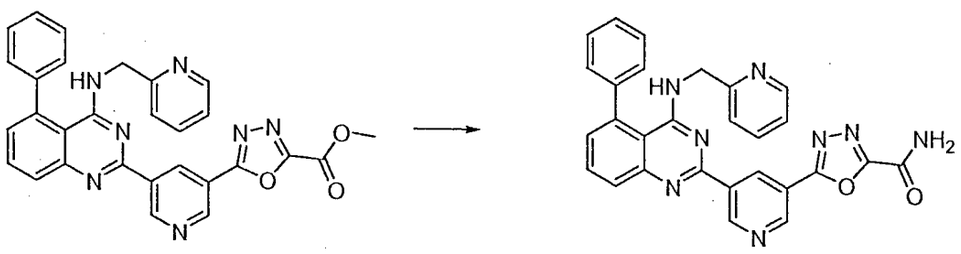
Step 1. Preparation of methyl 5-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)-1,3,4-oxadiazole-2-carboxylate



[00218] To a solution of 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinohydrazide (from Example 185, 0.30 g, 0.66 mmol) in DCM at 0 °C was added methyl 2-chloro-2-oxoacetate (0.062 mL, 0.66 mmol) and potassium carbonate (0.273 g, 1.90 mmol). Upon completion of addition, the mixture was stirred at RT for 16 h. After this time, water was added and the mixture was extracted into DCM, dried and concentrated. The resulting residue was dissolved in DCM. Triflic anhydride (0.187 mL, 1.1 mmol) and pyridine (0.149 mL, 1.8 mmol) were added and the resulting mixture was stirred at RT for 16 h. At the conclusion of this period, the

reaction mixture was quenched with water and extracted with DCM (100 mL). The DCM layer was washed with water and brine. Chromatographic purification provided methyl 5-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)-1,3,4-oxadiazole-2-carboxylate (270 mg, 78 % yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.81 (s, 1H), 9.17 (s, 1H), 9.09 (s, 1H), 8.24 (d, J = 4.4 Hz, 1H), 7.94 (d, J =7.2 Hz, 1H), 7.86 (t, J = 7.6 Hz, 1H),7.75-7.72 (t, J = 7.6 Hz, 3H), 7.59-7.51 (m, 5H), 7.34 (d, J =7.2 Hz, 2H), 7.24 (t, J =6.4 Hz, 1H), 6.98 (t, J = 3.2 Hz, 1H), 4.77 (d, J = 4.0 Hz, 2H). LCMS Method Q: retention time 1.39 min; [M+1] = 514.5; HPLC Method B: purity 98.1 %, retention time = 8.74 min.

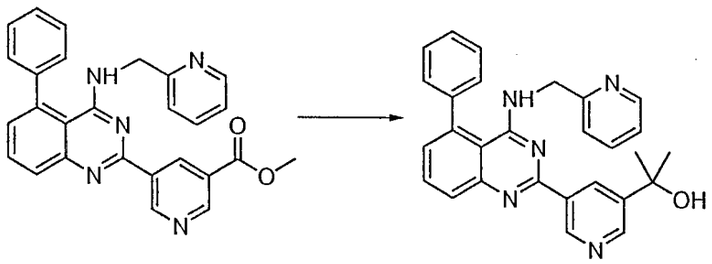
Step 2. Example 194



[00219] A solution of the methyl 5-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)-1,3,4-oxadiazole-2-carboxylate (0.0700 g, 0.136 mmol) in NH_3 (2.0 M in MeOH, 10 mL) was heated at 60 °C, in a sealed vessel for 4 h. After this time, the reaction mixture was allowed to cool to room temperature and the solvent was evaporated under reduced pressure to provide the crude product. The crude product was recrystallized from EtOAc/hexanes to provide Example 194 (0.06 g, 99 % yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.81 (s, 1H), 9.17 (s, 1H), 9.09 (s, 1H), 8.24 (d, J = 4.4 Hz, 1H), 7.94 (d, J =7.2 Hz, 1H), 7.86 (t, J = 7.6 Hz, 1H),7.75-7.72 (t, J = 7.6 Hz, 3H), 7.59-7.51 (m, 5H), 7.34 (d, J =7.2 Hz, 2H), 7.24 (t, J =6.4 Hz, 1H), 6.98 (t, J = 3.2 Hz, 1H), 4.77 (d, J = 4.0 Hz, 2H). LCMS Method Q: retention time 1.39 min; [M+1] = 499.50. HPLC Method B: purity 98.1 %, retention time = 8.74 min.

EXAMPLE 195

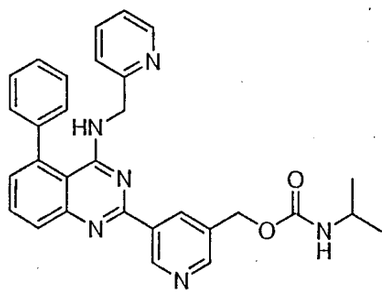
2-(5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)propan-2-ol



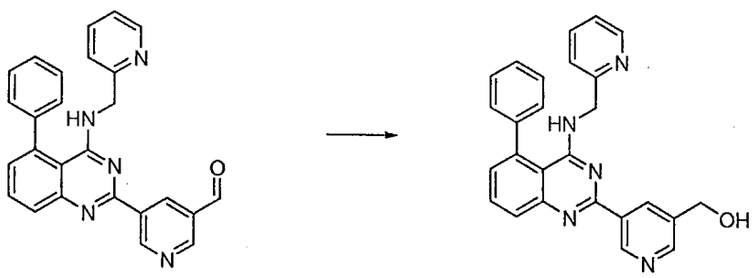
[00220] To a solution of methyl 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinate (from Example 43,0.30 g, 0.67 mmol) in THF (10 mL) was added methyl magnesium iodide (3.3 mL, 10 mmol) at 0 °C under nitrogen atmosphere. Upon the completion of addition, the reaction mixture was stirred at room temperature for 16 h. After this time, the reaction mixture was quenched with the addition of water and then extracted with ethyl acetate (50 mL). The combined organic extracts were washed successively with water and brine. The organic layer was dried, filtered and concentrated. The resulting residue was purified by column chromatography on silica gel (5 % methanol in dichloromethane) to afford Example 195 (0.090 g, 30 % yield) as an off white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.51 (s, 1H), 8.81 (s, 1H), 8.79 (s, 1H), 8.25 (d, 1H, J = 4.4 Hz), 7.92 (d, 1H, J = 8.4Hz), 7.85 (dt, 1H, J=7.2, 8Hz), 7.74 (m, 1H), 7.60-7.51(m, 5H), 7.34-7.31 (m, 2H), 7.29-7.22 (m, 1H), 7.24 (t, 1H, J = 4.8, 7.6 Hz), 6.80 (s, 1H), 5.36 (s, 1H), 4.75 (d, 2H, J-4Hz), 1.51(s,6H). HPLC Method B: purity 99.0 %, retention time = 7.26 min; LCMS Method E: retention time 1.8 min; [M+1] = 447.50.

EXAMPLE 196

(5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)methyl isopropylcarbamate

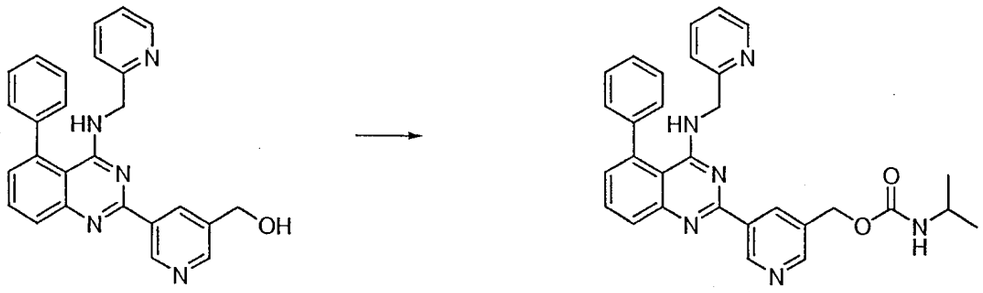


Step 1. Preparation of (5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)methanol



[00221] To a solution of 5-(5-phenyl-4-(pyridin-2-ylmethylamino) quinazolin-2-yl) nicotinaldehyde (from example 191, 1.0 g, 2.4 mmol) in ethanol (15 mL) was added $NaBH_4$ (0.28 g, 7.19 mmol). Upon completion of addition, the reaction mixture was stirred at RT for 4 h. After this time, a saturated solution of ammonium chloride was added and the resulting mixture was extracted into ethyl acetate. The organic layer was separated, dried, filtered and concentrated under reduced pressure to yield a residue. The residue was purified by silica gel column chromatography using 2 % methanol in DCM as the eluent to provide pure (5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)methanol (0.71 g, 71 % yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.51 (s, 1H), 8.72 (s, 1H), 8.63 (s, 1H), 8.23 (d, 1H, J = 4.8 Hz), 7.88 (dd, 1H, J = 7.6Hz, 8.4Hz), 7.85 – 7.80 (m, 1H), 7.73 (dt, 1H, J = 1.2 Hz, 7.6Hz), 7.61-7.48 (m, 5H), 7.33 (d, 2H, J =19.2 Hz), 7.27 (d, 1H, J =14 Hz), 7.23 (dt, 1H, J = 1.6, 7.2 Hz), 6.87 (t, 1H, J = 4.0 Hz, 1H), 5.47 (t, 1H, J=5.6), 4.75 (d, 2H, J-4Hz), 4.67 (d, 2H, J = 5.6Hz). LCMS Method U: retention time 1.46 min; [M+1] = 420.2; HPLC Method A2: purity 99.5 %, retention time = 5.77 min.

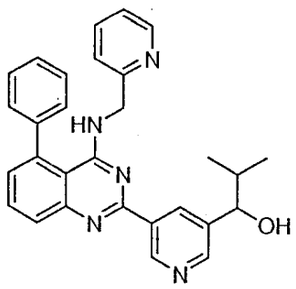
Step 2. Example 196

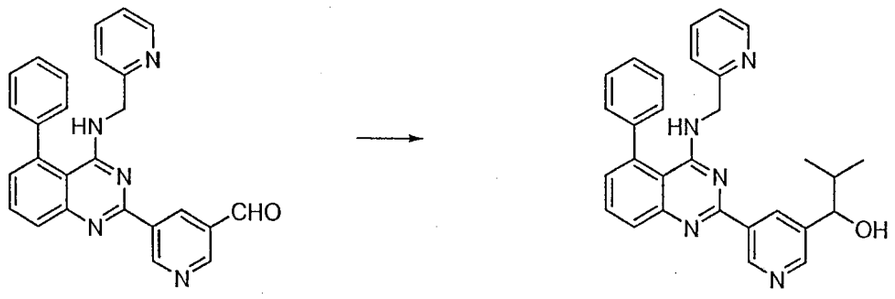


[00222] To a solution of (5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)methanol (0.050 g, 0.12 mmol) in DCM (2 mL) was added DMAP (0.014 g, 0.12 mmol) followed by isopropylisocyanate (0.010 g, 012 mmol) at 0 °C. Upon the completion of addition, the reaction mixture was slowly heated to 45 °C where it stirred for 8 h. At the conclusion of this period, the reaction mixture was washed with water and extracted with ethyl acetate. The combined organic extracts were dried, filtered, concentrated under reduced pressure to yield a residue. The residue purified by silica gel column chromatography (2 % MeOH in DCM) to provide Example 196 (30 mg, 50 % yield). ^{1}H NMR (400 MHz, DMSO-d6, δ): 9.59 (s, 1H); 8.75 (s, 1H); 8.70 (s, 1H); 8.24 (d, 1H, J = 4.8 Hz); 7.88 9dd, 1H, J = 1.2, 8Hz); 7.84 (t, 1H, J = 7.2 Hz); 7.73 (dt, 1H, J= 1.6, 7.6Hz); 7.60-7.49 (m, 5H); 7.38-7.29 (m, 3H); 7.23 (dd, 1H, J = 1.6, 7.2Hz); 6.87 (br s, 1H); 5.18 (br s, 1H); 4.75 (d, 2H, J = 4HZ); 3.72-3.60 (m, 1H); 1.08 (d, 6H, J = 6.4Hz). LCMS Method Y: retention time 2.00 min, [M+1] = 505.4; HPLC Method A1: purity 98.9 %, retention time = 8.12 min.

EXAMPLE 197

2-Methyl-1-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)propan-1-ol



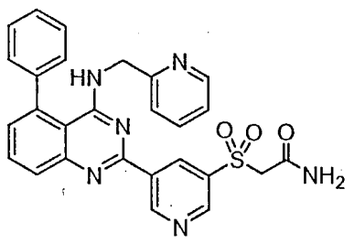


[00223] To a solution of 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinaldehyde (from example 191, 0.15 g, 0.35 mmol) in THF at -78 °C was added isopropyl magnesium chloride solution (2 M in THF, 10 eq). Upon completion of addition, the reaction mixture was allowed to reach room temperature. Once at the prescribed temperature, the reaction mixture was stirred for 16 h. After this time, the reaction mixture was quenched with a saturated solution of ammonium chloride (2 mL) and then extracted with ethyl acetate. The combined organic layers were dried, concentrated under reduced pressure, and purified by silica gel column chromatography (2% MeOH in DCM) to yield racemic Example 197 (20 mg, 12 % yield). The racemate was separated into the corresponding enantiomers using chiral HPLC to provide the pure Enantiomer 1(4 mg) and Enantiomer 2 (3.5 mg), respectively. CHIRAL HPLC: (CHIRAL PAK IC (250 X 4.6) mm, 5micron; mobile phase (85% hexane, 15% ethanol; flow rate: 1ml/min}. Enantiomer-1: ^{1}H NMR (400 MHz, DMSO-d6, δ): 9.51 (s, 1H); 8.69 (s, 1H); 8.60 (s, 1H); 8.26 (d, 1H, J = 4.4Hz); 7.90 (d, 1H, J = 7.6Hz); 8.55 (t, 1H, J = 7.2Hz); 7.73 (dt, 1H, J = 1.6, 7.6Hz); 7.61-7.50 (m, 4H); 7.38-7.30 (m, 2H); 7.24 (t, 1H, J = 9.2Hz); 6.81 (br s, 1H); 5.42 (d, 1H, J =4.4Hz); 4.74 (d, 2H, J = 4Hz); 4.45 (t, 1H, J = 4.8Hz); 2.00-2.90 (m, 1H); 0.92 (d, 3H, J =6.4Hz); 0.82 (t, 3H, J = 6.4Hz). LCMS Method T: retention time 1.78 min, [M+1] = 462.2; HPLC Method A1: purity 99.0%, retention time = 6.93 min. CHIRAL HPLC: retention time 19.78 {CHIRAL PAK IC (250 X 4.6) mm, 5micron; mobile phase (hexane (85), Ethanol (15); Flow rate: 1ml/min}. Enantiomer-2: ^{1}H NMR (400 MHz, DMSO-d6, δ): 9.51 (s, 1H); 8.69 (s, 1H); 8.60 (s, 1H); 8.26 (d, 1H, J = 4.4Hz); 7.90 (d, 1H, J = 7.6Hz); 8.55 (t, 1H, J = 7.2Hz); 7.73 (dt, 1H, J = 1.6, 7.6Hz); 7.61-7.50 (m, 4H); 7.38-7.30 (m, 2H); 7.24 (t, 1H, J = 9.2Hz); 6.81 (br s, 1H); 5.42 (d, 1H, J =4.4Hz); 4.74 (d, 2H, J = 4Hz); 4.45 (t, 1H, J = 4.8Hz); 2.00-2.90

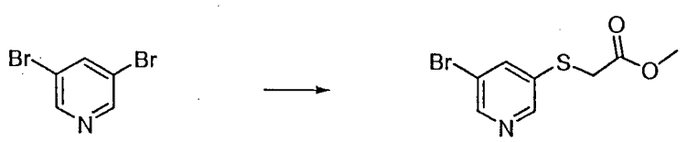
(m, 1H); 0.92 (d, 3H, J =6.4Hz); 0.82 (t, 3H, J = 6.4Hz). LCMS Method T: retention time 1.78 min, [M+1] = 462.2; HPLC Method A1: purity 96.9%, retention time = 6.93 min. CHIRAL HPLC: retention time 22.02 {CHIRAL PAK IC (250 X 4.6) mm, 5micron; mobile phase (hexane (85), Ethanol (15); Flow rate: 1ml/min}.

EXAMPLE 198

2-(5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-ylsulfonyl)acetamide

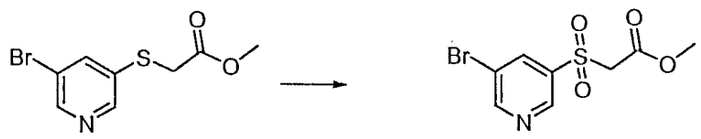


Step 1. Preparation of methyl 2-(5-bromopyridin-3-ylthio)acetate



[00224] To a solution of sodium hydride (0.518 g, 21.0 mmol) in DMF (5 mL) at 0 °C was added dropwise a solution of methylthioglycolate (2 g, 18 mmol) in DMF (6 mL). Upon completion of addition, the reaction mixture was stirred at RT for 30 min. After this time, a solution of 3,5-dibromopyridine (4.46 g, 18 mmol) in DMF (10 mL) was added dropwise. The resulting reaction mixture was allowed stir at RT for 16 h. At the conclusion of this period, the reaction mixture was quenched by the addition of ice and the resulting slurry was extracted with ethyl acetate. The combined organic layers were dried and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (1.5 % methanol in DCM) to yield methyl 2-(5-bromopyridin-3-ylthio)acetate (1.2 g, 24 % yield). LCMS Method A: retention time 1.49 min; [M+1] = 262.

Step 2. Preparation of methyl 2-(5-bromopyridin-3-ylsulfonyl)acetate



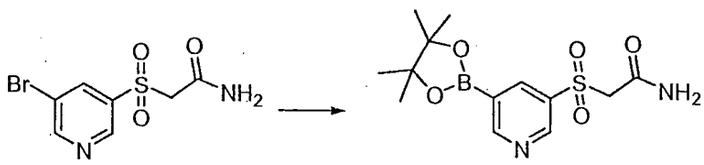
[00225] To a solution of methyl 2-(5-bromopyridin-3-ylthio)acetate (1.2 g, 4.6 mmol) in 3:1 MeOH:H_2O (12 mL) was added oxone (2.8 g, 4.6 mmol). Upon completion of addition, the reaction mixture was stirred at RT for 5 h. At the conclusion of this period, the reaction mixture was concentrated under reduced pressure and then extracted with DCM. The combined organic layers were dried and concentrated under reduced pressure to yield a residue. The residue was purified by silica gel column chromatography (1.5 % methanol in DCM) to yield methyl 2-(5-bromopyridin-3-ylsulfonyl)acetate (0.6 g, 46 % yield). ^{1}H NMR (400 MHz, DMSO-d6, δ): 9.11 (d, 1H, J = 2Hz); 9.02 (d, 1H, J = 2Hz); 8.57 (t, 1H, J = 2Hz); 4.95 (s, 2H); 3.63 (s, 3H). LCMS Method T: retention time 1.12 min; [M+1] = 294.0.

Step 3. Preparation of 2-(5-bromopyridin-3-ylsulfonyl)acetamide



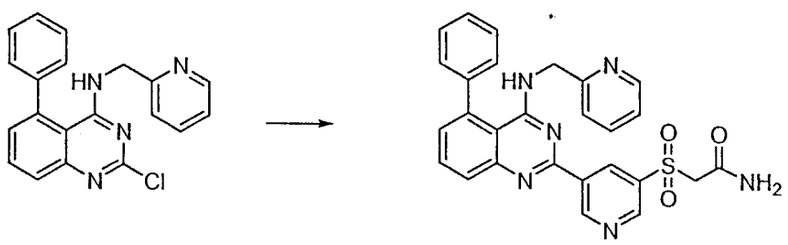
[00226] To a solution of methyl 2-(5-bromopyridin-3-ylsulfonyl)acetate (0.2 g, 0.67 mmol) was added 5 % ammonia in methanol (10 mL). Upon completion of addition, the reaction mixture was stirred at 60 $^{\circ}$C for 4 h. After this time, the reaction mixture was allowed to cool to room temperature. Once at the prescribed temperature, the reaction mixture was concentrated under reduced pressure to afford 2-(5-bromopyridin-3-ylsulfonyl)acetamide (0.2 g) as a white solid. LCMS Method W: retention time 0.92 min; [M-1] = 277.0.

Step 4. Preparation of 2-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-ylsulfonyl)acetamide



[00227] A mixture 2-(5-bromopyridin-3-ylsulfonyl)acetamide (0.2 g, 0.7 mmol), bis(pinacolato)diboron (0.27 g, 1 mmol) and potassium acetate (0.2 g, 2.1 mmol) in 1,4-dioxane (10 mL) was degassed with nitrogen for 15 min. After this time, (1,1'-bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (0.028 g, 0.035mmol) was added and the resulting mixture was again degassed for 10 min. with nitrogen. The reaction mixture was then heated in the microwave at 100 °C for 16 h. At the conclusion of this period, the reaction mixture was filtered through celite and the filtrate was concentrated under reduced pressure to provide 2-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-ylsulfonyl)acetamide (0.170 g), which was used without further purification.

Step 5. Example 198

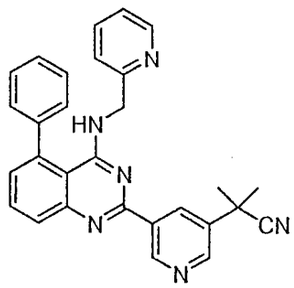


[00228] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (from example 1, step 4, 0.182 g, 0.52 mmol) in 1,4-dioxane (6 mL) and H_2O (1.2 mL) under nitrogen was added 2-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-ylsulfonyl)acetamide (0.170 g, 0.57 mmol), and potassium carbonate (0.215 g, 1.56 mmol). Upon completion of addition, the reaction mixture was degassed with nitrogen for 15 min. After this time, (1,1'-bis(diphenylphosphino)-ferrocene)palladium (II) chloride dichloromethane complex (0.042 g, 0.052 mmol) was added. The resulting mixture was again degassed with nitrogen for 10 min. At the conclusion of this period, the reaction mixture was stirred at 100 °C for 16 h, then

allowed to cool to room temperature and quenched by the addition of water. Upon the completion of addition, the reaction mixture was transferred to a separation funnel and the aqueous layer was extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting concentrate was purified by column chromatography to afford Example 198 (0.020 g, 8 % yield). ^{1}H NMR (400 MHz, DMSO-d6, δ): 9.89 (s, 1H); 9.17 (s, 1H); 9.14 (s, 1H); 8.25 (s, 1H); 7.96 (dd, 1H, J = 1.6, 4.4Hz); 7.88 (dd, 1H, J = 7.2, 8.4Hz); 7.73 (dd, 1H, J = 2, 7.6Hz); 7.61-7.50 (m, 5H); 7.45 (br s, 1H); 7.39-7.33 (m, 2H); 7.24 (t, 1H, J = 2.4Hz); 6.96 (br s, 1H); 4.77 (d, 2H, J = 4Hz); 4.49 (s, 2H). LCMS Method Y: retention time 1.83 min, [M-1] = 509.0; HPLC Method A1: purity 96.2 %, retention time = 6.79 min.

EXAMPLE 199

2-Methyl-2-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)propanenitrile



Step 1. Preparation of 3-bromo-5-chloromethyl-pyridine



[00229] To a solution of (5-bromo-pyridin-3-yl)-methanol (0.5 g, 2.68 mmol) in DCM (10 mL) was added thionyl chloride (0.5 mL). The resulting solution was stirred at room temperature for 2 h. After this time, the reaction mixture was quenched with water and extracted into DCM. The organic extracts were washed

with brine filtered and concentrated under reduced pressure to give 3-bromo-5-chloromethyl-pyridine (0.45 g, 82 %), which was used in the next step without further purification.

Step 2. Preparation of 2-(5-bromopyridin-3-yl) acetonitrile



[00230] Potassium cyanide (0.21 g, 3.27 mmol) was added to a solution of 3-bromo-5-chloromethyl-pyridine (0.45 g; 2.18 mmol) in DMF (10 mL). Upon completion of addition, the reaction mixture was stirred at room temperature for 16 h. After this time, the reaction mixture was quenched with water and extracted with ethyl acetate. The organic phase was washed with water and brine, dried over Na_2SO4, filtered and evaporated. The resulting residue was purified by silica gel column chromatography (10 % ethyl acetate in hexane) to provide 2-(5-bromopyridin-3-yl) acetonitrile (200 mg, 46.5 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.68 (d, 1H, J = 2Hz), 8.51 (d, 1H, J = 2Hz), 7.88 (t, 1H, J = 2Hz), 3.77 (s, 2H).

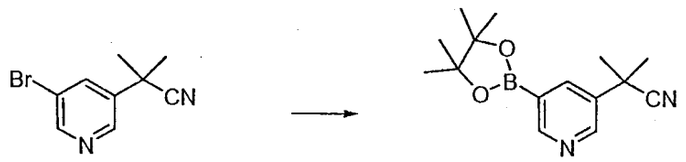
Step 3. Preparation of 2-(5-bromopyridin-3-yl)-2-methylpropanenitrile



[00231] To a suspension of NaH (95 %, 0.17 g, 7.1 mmol) in THF was added a solution of 2-(5-bromopyridin-3-yl)acetonitrile (0.7 g, 3.0 mmol) in THF (5 mL) at 0 °C and the resulting reaction mixture stirred at RT for 30 min. At the conclusion of this period, methyl iodide (0.66 mL, 8.9 mmol) was added and then stirring continued for an additional 16 h. After this time, the reaction mixture was quenched by the addition of saturated ammonium chloride solution and then extracted into ethyl acetate. The combined organic portions were concentrated under reduced pressure

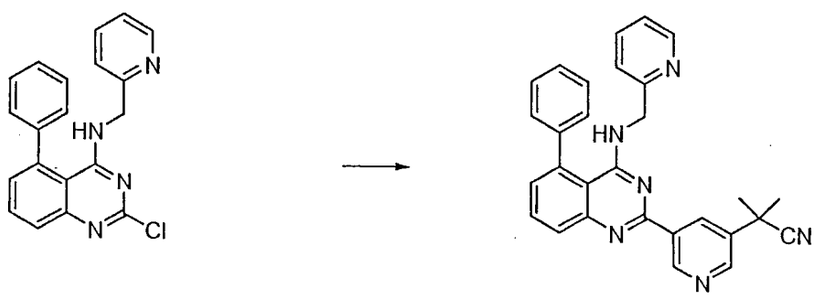
and the resulting residue was purified by flash column chromatography (15 % ethyl acetate in hexanes) to yield 2-(5-bromopyridin-3-yl)-2-methylpropanenitrile (0.35 g, 56 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.67 (d, 1H, J = 2Hz),8.45 (d, 1H, J = 2Hz), 7.73 (t, 1H, J = 2Hz), 2.44 (s, 3H), 2.28 (s, 3H).

Step 4. Preparation of 2-methyl-2-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)propanenitrile



[00232] A mixture of 2-(5-bromopyridin-3-yl)-2-methylpropanenitrile (0.4 g, 1.77 mmol), bis(pinacolato)diboron (0.67 g, 2.65 mmol) and potassium acetate (0.69 g, 7.04 mmol) in 1,4-dioxane (15 mL) was degassed with nitrogen for 15 min. After this time, (1,1'-bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (0.11 g, 0.15 mmol) was added. The reaction mixture was again degassed for 10 min with nitrogen and then heated in the microwave at 120 °C for 45 min. At the conclusion of this period, the reaction mixture was filtered through celite and the filtrate was concentrated under reduced pressure to provide 2-methyl-2-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)propanenitrile (0.53 g), which was used without further purification.

Step 5. Example 199

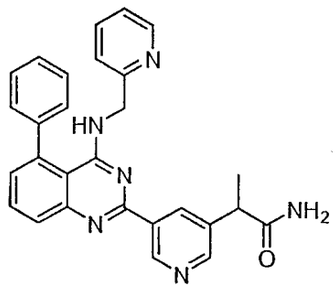


[00233] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (from example 1, step 4, 0.4 g, 1 mmol) in 1,4-dioxane (15 mL) and H_2O (1 mL) under nitrogen was added 2-methyl-2-(5-(4,4,5,5-tetramethyl-1,3,2-

dioxaborolan-2-yl)pyridin-3-yl)propanenitrile (0.5 g, 2 mmol) and potassium carbonate (0.48 g, 3.5 mmol). Upon completion of addition, the mixture was degassed with nitrogen for 15 min. At the conclusion of this period, (1,1'-bis (diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (85 mg, 0.11 mmol) was added and the reaction mixture was again degassed with nitrogen for 10 min. After this time, the reaction mixture was stirred at 95 °C for 16 h. At the conclusion of this period, the reaction mixture was allowed to cool to room temperature and then quenched by the addition of water. Upon completion of addition, the reaction mixture was transferred to a separation funnel and the aqueous layer was extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (2 % methanol in dichloromethane) to afford Example 199 (0.38 g, 72 % yield) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.61 (s, 1H), 8.92 (s, 1H), 8.88 (s, 1H), 8.24 (d, 1H, J = 4.4 Hz), 7.93 (dd, 1H, J =1.2 Hz, 4.4Hz), 7.84 (t, 1H, J = 8 Hz),7.73 (dt, 1H, J = 1.6, 8Hz), 7.63-7.50 (m, 5H), 7.36-7.30 (m, 2H), 7.24 (t, 1H, J = 5.6Hz), 6.84 (br s, 1H), 4.75 (d, 2H, J = 4.0 Hz), 1.84 (s, 6H). LCMS Method Y: retention time 2.04 min; [M+1] = 457.0; HPLC Method A1: purity 99.1 %, retention time = 8.39 min.

EXAMPLE 200

2-(5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)propanamide

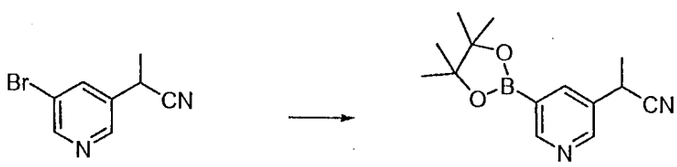


Step 1. Preparation of 2-(5-bromopyridin-3-yl)propanenitrile



[00234] To a suspension of NaH (95 %, 113 mg, 4.70 mmol) in DMF was added a solution of 2-(5-bromopyridin-3-yl)acetonitrile (from example 199, 0.8 g, 4 mmol) in DMF. Upon completion of addition, the reaction mixture was stirred at RT for 30 min. After this time, methyl iodide (0.3 mL, 4 mmol) was added and the stirring continued for an additional 4 h. At the conclusion of this period, the reaction mixture was quenched by addition of saturated ammonium chloride solution and then extracted into ethyl acetate. The combined organic portions were concentrated under reduced pressure and the resulting residue was purified by flash column chromatography (30 % EtOAc in hexanes) to yield racemic 2-(5-bromopyridin-3-yl)propanenitrile (200 mg, 24 %). ^{1}H NMR (400 MHz, $CDCL_3$) δ (ppm): 8.67 (d, 1H, J = 2Hz); 8.53 (d, 1H, J = 5Hz); 7.88 (t, 1H, J = 5Hz); 3.94 (q, 1H, J = 7.6 Hz); 1.69 (d, 3H, J = 7.6Hz). LCMS Method Y: retention time 1.54 min; [M+1] = 212.6.

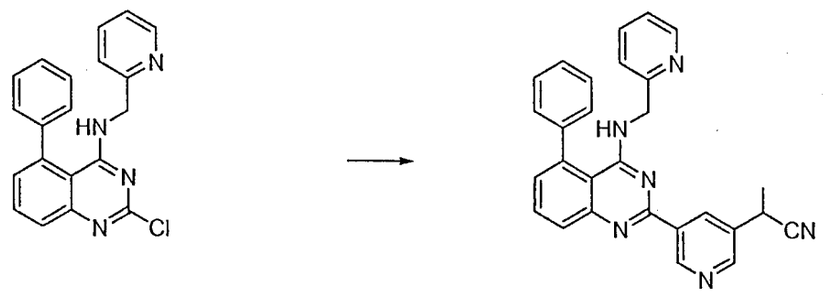
Step 2. Preparation of 2-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)propanenitrile



[00235] A mixture of 2-(5-bromopyridin-3-yl)propanenitrile (0.1 g, 0.5 mmol), bis(pinacolato)diboron (0.18 g, 0.70 mmol) and potassium acetate (0.19 g, 1.9 mmol) in 1,4-dioxane (8 mL) was degassed with nitrogen for 15 min. After this time, (1,1'-bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (28 mg, 0.038 mmol) was added and the resulting mixture was again degassed for 10 min. with nitrogen. At the conclusion of this period, the reaction mixture was heated in the microwave at 120 °C for 45 min. After this time, the reaction mixture was filtered through celite and the filtrate was concentrated under reduced pressure to provide racemic 2-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-

yl)propanenitrile (0.12 g), which was used without further purification. LCMS Method Y: retention time 1.83 min; [M+1] = 258.8.

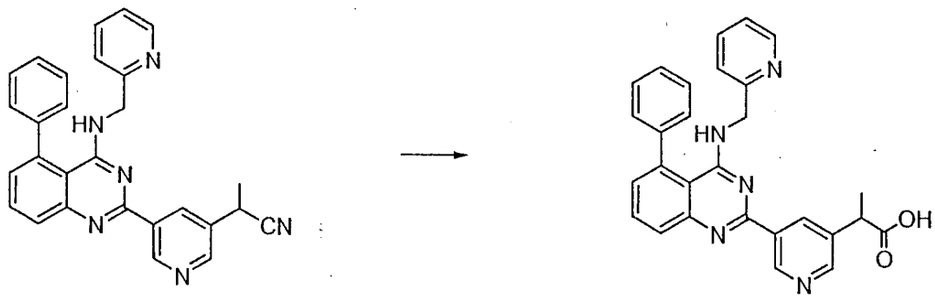
Step 3. Preparation of 2-(5-(5-phenyl-4-(pyridin-2-ylmethylamino) quinazolin-2-yl)pyridin-3-yl)propanenitrile



[00236] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (from example 1, step 4, 0.12 g, 0.5 mmol) in 1,4-dioxane (8 mL) and H_2O (0.55 mL) under nitrogen was added 2-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)propanenitrile (0.120 g, 0.4 mmol) and potassium carbonate (0.14 g, 1 mmol). The resulting mixture was degassed with nitrogen for 15 min. After this time, (1,1'-bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (0.26 mg, 0.036 mmol) was added and the reaction mixture was again degassed with nitrogen for 10 min. At the conclusion of this period, the reaction mixture was stirred at 95 °C for 16 h. The reaction mixture was then allowed to cool to room temperature. Once at the prescribed temperature, the reaction mixture was quenched by the addition of water and then transferred to a separation funnel. The aqueous layer was extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting concentrate was purified by silica gel column chromatography using 1 % methanol in DCM to afford racemic 2-(5-(5-phenyl-4-(pyridin-2-ylmethylamino) quinazolin-2-yl)pyridin-3-yl)propanenitrile (95 mg, 63 % yield) as an off white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.60 (s, 1H), 8.80 (d, 1H, J = 2Hz); 8.77 (s, 1H); 8.26 (d, 1H, J = 6Hz); 7.92 (dd, 1H, J = 1.2, 6.8Hz); 7.85 (t, 1H, J = 6.8Hz); 7.73 (dt, 1H, J = 1.6, 7.6Hz); 7.58-7.52 (m, 5H);

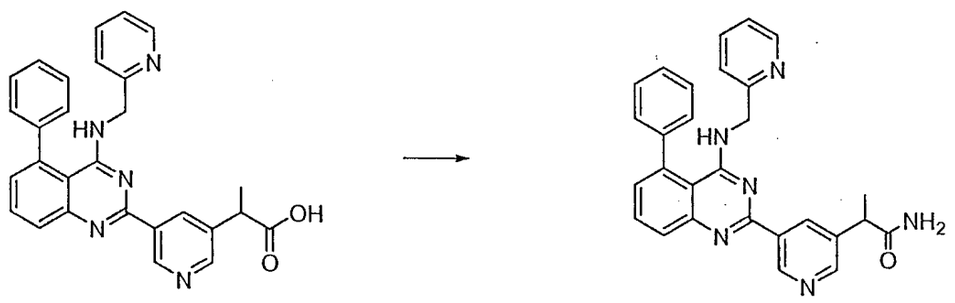
7.34-7.32 (m, 2H); 7.24 (t, 1H, 7.2Hz); 6.86 (t, 1H, *J* = 4Hz); 4.76 (d, 2H, *J* = 4.4Hz); 4.59 (q, 1H, *J* = 7.2Hz); 1.68 (d, 3H, 7.2Hz). LCMS Method Y: retention time 1.68 min, [M+1] = 443.2.

Step 4. Preparation of 2-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)propanoic acid



[00237] To a solution of racemic of 2-(5-(5-phenyl-4-(pyridin-2-ylmethylamino) quinazolin-2-yl)pyridin-3-yl) propanenitrile (0.08 g, 0.18 mmol) in ethanol/water(3:3 mL) was added solid NaOH (52 mg, 1.1 mmol). Upon completion of addition, the reaction mixture was heated at 95 °C for 16 h. After this time, the reaction mixture allowed to cool to RT and then water was added (5 mL). Upon completion of addition, 1.0 N HCl was added to the reaction mixture to adjust the pH to 6-7. Once at the prescribed pH, the aqueous portion was extracted with ethyl acetate. The combined organic extracts were dried, filtered and concentrated under reduced pressure to yield racemic 2-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)propanoic acid (32 mg, 39 % yield).

Step 5. Example 200

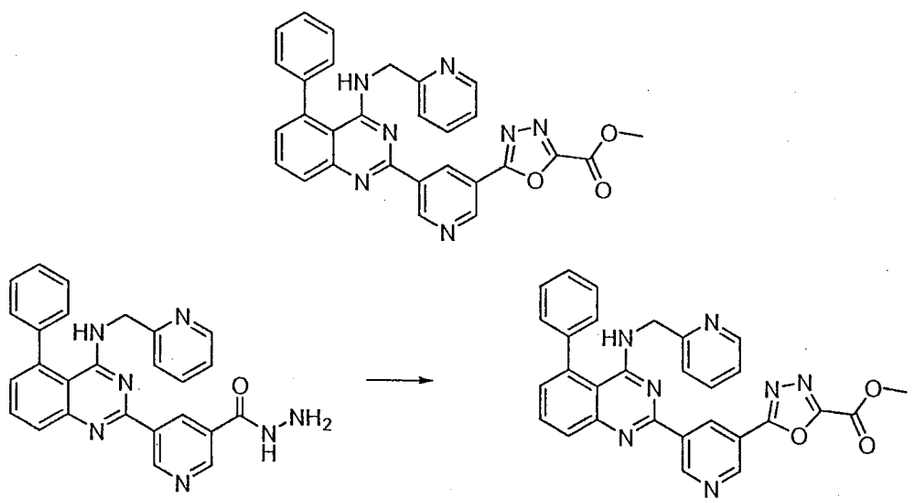


[00238] To a solution of racemic 2-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)propanoic acid (0.08 g, 0.2 mmol) in DMF (1.5 mL) was added EDCI (0.04 g, 0.2 mL), HOBt (0.028 g, 0.20 mmol) and DIPEA (0.2 mL, 0.7 mmol) followed by ammonium chloride (0.03 g, 0.7 mmol). The reaction mixture was stirred at room temperature for 2 h. After this time, the reaction mixture was washed and then extracted with ethyl acetate. The combined organic extracts were dried, filtered and concentrated under reduced pressure. The resulting residue was purified by flash silica gel column chromatography (5 % methanol in dichloromethane) to obtain racemic Example 200 (35 mg, 43 % yield) as an off-white solid. The enantiomers were separated by Chiral HPLC (CHIRAL HPLC: CHIRAL PAK IC (250 X 4.6)mm, 5micron; mobile phase 85% hexane , 15% ethanol ; Flow rate: 1ml/min}). Enantiomer-1: ^{1}H NMR (400 MHz, DMSO-d6, δ): 9.50 (s, 1H); 8.70 (s, 1H); 8.65 (s, 1H); 8.25 (d, J=4.8Hz, 1H), 7.91 (dd, J=1.2Hz, 8.4Hz, 1H), 7.84 (t, 7.2Hz, 1H), 7.72 (dt, J=1.6Hz, 7.6Hz, 1H), 7.62-7.50 (m, 6Hz), 7.36-7.30 (m, 2H), 7.23 (dd, J=5.2Hz, 6.2Hz, 1H), 6.98 (s, 1H), 6.83 (brs, 1H), 4.74 (d, J=4Hz, 2H), 3.78 (t, J=7.7Hz, 1H), 1.44 (d, J=7.2Hz, 3H). LCMS Method Y: retention time 1.78 min; [M+1] = 461.0; HPLC Method A1: purity 99.8 %, retention time = 6.04 min. CHIRAL HPLC: retention time 15.43 {CHIRAL PAK IC (250 X 4.6)mm, 5micron; mobile phase 85% hexane , 15% ethanol; Flow rate: 1ml/min}. Enantiomer-2: ^{1}H NMR (400 MHz, DMSO-d6, δ): 9.50 (s, 1H); 8.70 (s, 1H); 8.65 (s, 1H); 8.25 (d, J=4.8Hz, 1H), 7.91 (dd, J=1.2Hz, 8.4Hz, 1H), 7.84 (t, 7.2Hz, 1H), 7.72 (dt, J=1.6Hz, 7.6Hz, 1H), 7.62-7.50 (m, 6Hz), 7.36-7.30 (m, 2H), 7.23 (dd, J=5.2Hz, 6.2Hz, 1H), 6.98 (s, 1H), 6.83 (brs, 1H), 4.74 (d, J=4Hz, 2H), 3.78 (t, J=7.7Hz, 1H), 1.44 (d, J=7.2Hz, 3H). LCMS Method Y: retention time 1.78 min; [M+1] = 461.0; HPLC Method A1: purity 99.6 %, retention time = 6.06 min. CHIRAL HPLC: retention

time 19.08 {CHIRAL PAK IC (250 X 4.6)mm, 5micron; mobile phase 85% hexane , 15% ethanol; Flow rate: 1ml/min}.

EXAMPLE 201

Methyl 5-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)-1,3,4-oxadiazole-2-carboxylate

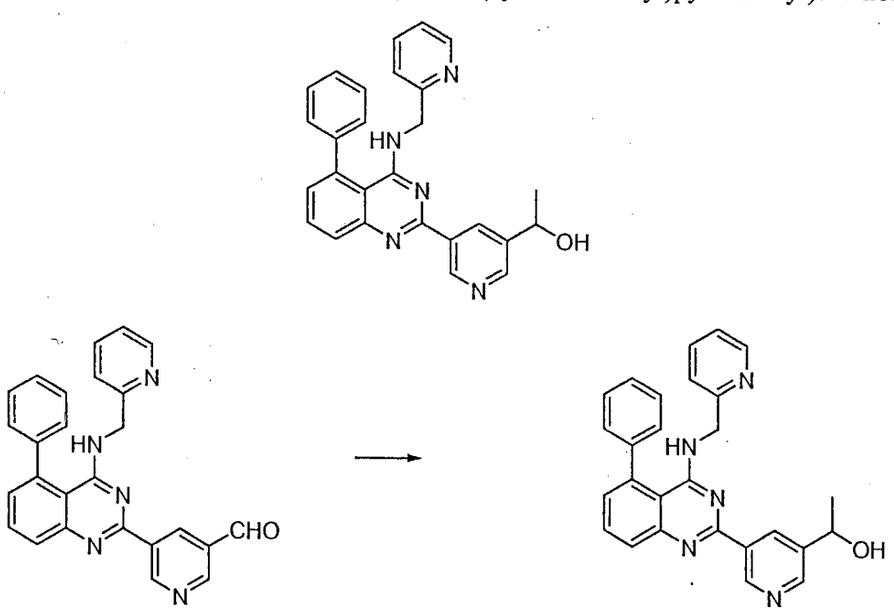


[00239] To a solution of 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinohydrazide (from example 185, 0.3 g, 0.66 mmol) in DCM (3 mL) at 0 °C was added methyl 2-chloro-2-oxoacetate (0.062 mL, 0.66 mmol) and potassium carbonate (0273 g, 1.90 mmol). Upon completion of addition, the reaction mixture was stirred at RT for 16 h. After this time, water was added (2 mL) and the reaction mixture was extracted into DCM. The combined organic portions were dried and concentrated under reduced pressure. The resulting residue was dissolved in DCM (3 mL) and trifluoromethanesulfonic anhydride (0.19 mL, 1.1 mmol) and pyridine (0.149 mL, 1.80 mmol) were added. Upon completion of addition, the reaction mixture was stirred at RT for 16 h. At the conclusion of this period, the reaction mixture was quenched by the addition of water and then extracted with DCM. The combined organic portions were washed successively with water and brine, dried, filtered and concentrated under reduced pressure to yield a residue. The residue was purified using flash column chromatography (2 % methanol in dichloromethane) to yield Example 201 (270 mg, 35 % yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.87 (s, 1H0; 9.36 (s, 1H0; 9.32 9s, 1H); 8.26 (d, 1H, J = 4.4Hz),

7.98 (dd, 1H, J = 1.2, 8.4Hz); 7.87 (dd, 1H, J = 1.4, 4Hz); 7.74 (dt, 1H, J 1.6, 7.6Hz); 7.62-7.50 (m, 5H); 7.39-7.31 (m, 2H); 7.24 (dd, 1H, J = 5.2, 6.8Hz); 6.95 (br t, 1H, J = 4.4Hz); 4.77 (d, 2H, J = 4Hz); 4.05 (s, 3H). LCMS Method Y: retention time 2.07 min; [M+1] = 516.0; HPLC Method A1: purity 96.4 %, retention time = 8.75 min.

EXAMPLE 202

1-(5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)ethanol

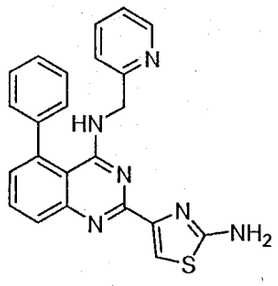


[00240] To a solution of 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinaldehyde (from example 191, 0.3 g, 0.7 mmol) in THF (5 mL) at 0 °C was added methylmagnesium bromide solution (3 M in THF, 0.7 mL, 2 mmol). Upon completion of addition, the reaction mixture was stirred at room temperature for 5 h. After this time, the reaction mixture was quenched by the addition of saturated solution of ammonium chloride (2 mL) and then extracted into ethyl acetate. The combined organic layers were dried, filtered concentrated to yield a residue. The residue purified by column chromatography to yield racemic Example 202 (20 mg, 7 % yield), which was separated into the corresponding enantiomers by chiral HPLC {CHIRAL PAK IC 250 X 4.6mm, 5micron; mobile phase 85% hexane , 15% ethanol; Flow rate: 1ml/min} to provide pure Enantiomer 1 (11mg) and Enantiomer 2 (12 mg),

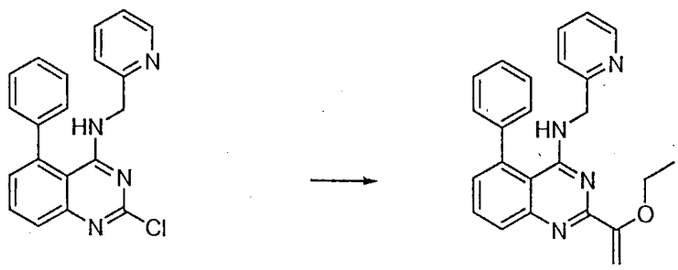
respectively. Enantiomer 1: ^{1}H NMR (400 MHz, DMSO-d6, δ): 9.50 (d, 1H, J = 2Hz); 8.73 (s, 1H); 8.65 (d, 1H, J = 2Hz); 8.24 (d, 1H, J = 4.8Hz); 7.90 (dd, 1H, J = 1.2, 8.4Hz); 7.83 (dd, 1H, J = 7.2, 8.4Hz); 7.71 (dt, 1H, J = 1.6, 7.6Hz); 7.60-7.49 (m, 5H); 7.38-7.27 (m, 2H); 7.23 (dd, 1H, J =3.2, 6.8Hz); 6.82 (br t, 1H, J = 4Hz); 5.45 (d, 2H, J = 4Hz); 4.92 (t, 1H, J = 3.6Hz); 4.74 (d, 2H, J = 4Hz); 1.45 (d, 3H, J = 6.8Hz). LCMS Method V: retention time 1.60 min, [M+1] = 434.2; HPLC Method A1: purity 99.8 %, retention time = 6.30 min. CHIRAL HPLC: retention time 16.27 {CHIRAL PAK IC (250 X 4.6)mm, 5micron; mobile phase 85% hexane , 15% ethanol; Flow rate: 1ml/min}. Enantiomer 2: ^{1}H NMR (400 MHz, DMSO-d6, δ): 9.50 (d, 1H, J = 2Hz); 8.73 (s, 1H); 8.65 (d, 1H, J = 2Hz); 8.24 (d, 1H, J = 4.8Hz); 7.90 (dd, 1H, J = 1.2, 8.4Hz); 7.83 (dd, 1H, J = 7.2, 8.4Hz); 7.71 (dt, 1H, J = 1.6, 7.6Hz); 7.60-7.49 (m, 5H); 7.38-7.27 (m, 2H); 7.23 (dd, 1H, J =3.2, 6.8Hz); 6.82 (br t, 1H, J = 4Hz); 5.45 (d, 2H, J = 4Hz); 4.92 (t, 1H, J = 3.6Hz); 4.74 (d, 2H, J = 4Hz); 1.45 (d, 3H, J = 6.8Hz). LCMS Method T: retention time 1.61 min, [M+1] = 434.2; HPLC Method A1: purity 96.8 %, retention time = 6.23 min. CHIRAL HPLC: retention time 21.02 {CHIRAL PAK IC (250 X 4.6)mm, 5micron; mobile phase 85% hexane , 15% ethanol; Flow rate: 1ml/min}.

EXAMPLE 203

4-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)thiazol-2-amine

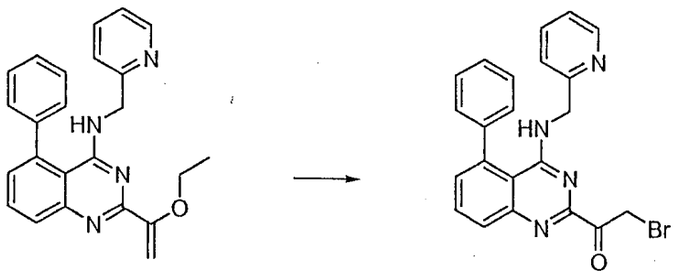


Step 1. Preparation of 2-(1-ethoxyvinyl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine



[00241] To 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine(1.0 g, 2.88 mmol) was added 1,4-dioxane (15 mL) and the resulting solution degassed with nitrogen. $Pd(TPP)_2Cl_2$ (0.202 g, 0.288 mmol) and tributyl(1-ethoxyvinyl)stannane (5.2 g, 14 mmol) were added under a nitrogen stream and the reaction mixture was heated to 90 °C where it stirred for 16 h. After this time, the reaction mixture was allowed to cool to room temperature. Once at the prescribed temperature, the reaction mixture was concentrated under reduced pressure and the resulting residue was purified by neutral alumina column chromatography (20% ethyl acetate, hexane) to yield 2-(1-ethoxyvinyl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (940 mg, 85 % yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.23 (d, 1H, J = 4.4 Hz), 7.75-7.85 (m, 2H), 7.70 (dt, 1H, J = 2, 7.6 Hz), 7.45-7.58 (m, 5H), 7.20-7.30 (m, 3H), 6.61 (br s, 1H), 4.61 (s, 1H), 4.60 (d, 2H, J = 4Hz), 3.94 (q, 2H, J = 6.8 Hz), 1.40 (t, 3H, J = 6.8 Hz). LCMS Method Y: retention time 1.952 min, [M+1] = 383.2.

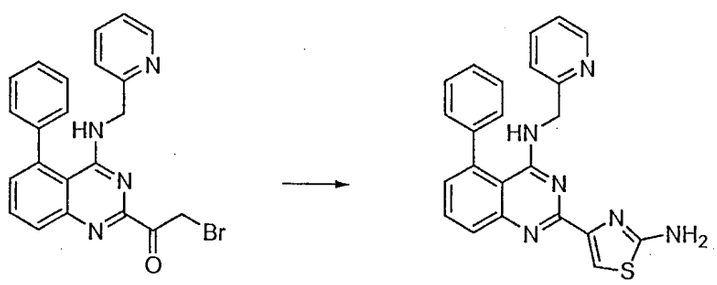
Step 2. Preparation of 2-bromo-1-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)ethanone



[00242] N-bromosuccinimide (0.55 g, 3.1 mmol) was added to 1,4-dioxane/water (3:1) (20 mL). 2-(1-Ethoxyvinyl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.59 g, 1.5 mmol) was then added in small portions at 0 °C. Upon completion

of addition, the reaction mixture was stirred at room temperature for 20 min. After this time, water was added and the aqueous portion was extracted twice with DCM. The combined organic layers were dried, filtered and evaporated under reduced pressure to yield 2-bromo-1-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)ethanone (600 mg, 69 % purity by LCMS), which was used without further purification. LCMS Method Y: retention time 1.996 min, [M+1] = 433.

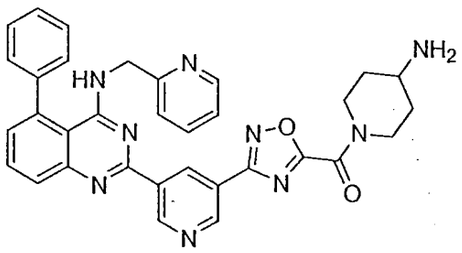
Step 3. Example 203



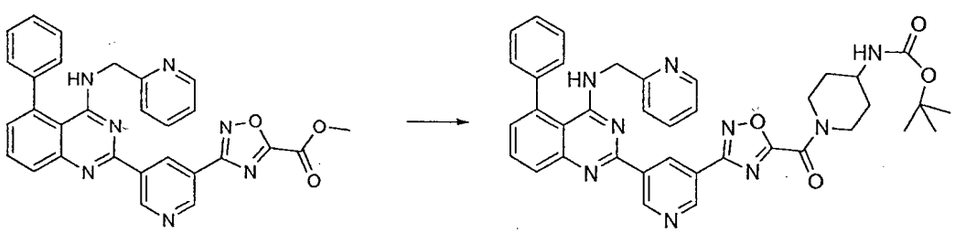
[00243] To a solution of 2-bromo-1-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)ethanone (75 mg, 0.17 mmol) in ethanol (7 mL) was added thiourea (14 mg, 0.17 mmol) and the reaction mixture heated to 70 °C for 1 h. After this time, the ethanol was evaporated under reduced pressure and DCM (25 mL) was added. Upon the completion of addition, the organic portion was washed with 10 % sodium bicarbonate solution and the aqueous layer was extracted with DCM (2x20 mL). The combined organic phases were dried and evaporated under reduced pressure to yield a residue. The residue was purified by silica gel chromatography (8 % methanol in dichloromethane) to provide Example 203 (25mg, 35%) as a black semi-solid. ^{1}H NMR (400 MHz, DMSO-d6, δ): 8.24 (d, 1H, J = 4.8Hz); 7.80-7.67 (m, 3H); 7.45-7.59 (m, 6H); 7.20-7.30 (m, 3H); 7.07 (s, 2H); 6.56 (br s, 1H); 4.65 (d, 2H, J = 4.4Hz). LCMS Method V: retention time 1.59 min, [M+1] = 411.2; HPLC Method A1: purity 97.6 %, retention time = 6.52 min.

EXAMPLE 204

(4-Aminopiperidin-1-yl)(3-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)-1,2,4-oxadiazol-5-yl)methanone

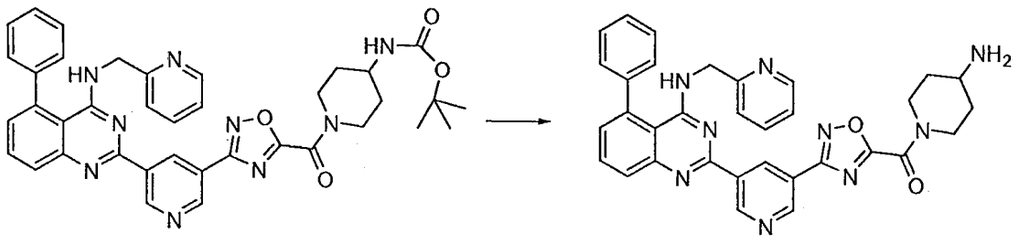


Step 1. Preparation of tert-butyl 1-(3-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)-quinazolin-2-yl)pyridin-3-yl)-1,2,4-oxadiazole-5-carbonyl)piperidin-4-ylcarbamate



[00244] To a solution of methyl 3-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)-1,2,4-oxadiazole-5-carboxylate (from example 187, 0.2 g, 0.38 mmol) in ethanol (10 mL) was added 4-(Boc-amino)piperidine (0.389 g, 1.90 mmol). Upon completion of addition, the reaction mixture was heated to 80 °C where it stirred for 16 h. At the conclusion of this period, the ethanol was evaporated and the resulting residue was purified by flash silica gel column chromatography (1.6 % methanol in DCM) to yield tert-butyl 1-(3-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)-1,2,4-oxadiazole-5-carbonyl)piperidin-4-ylcarbamate (0.1 g, 38 % yield) as yellow solid. LCMS Method T: retention time 2.08 min; [M+1] = 684.2.

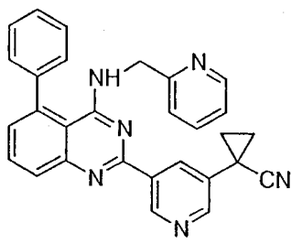
Step 2. Example 204



[00245] To a solution of tert-butyl 1-(3-(5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)-1,2,4-oxadiazole-5-carbonyl)piperidin-4-ylcarbamate (0.1 g, 0.1 mmol) in ether (3 mL) was added ether HCl (2 mL). The reaction mixture was stirred at RT for 16 h. After this time, a precipitate formed and the solution was decanted from the reaction mixture. The resulting solid was recrystallized from ether to yield Example 204 (0.022 g, 26 % yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.54 (s, 1H), 8.26 (d, 1H, J = 4Hz); 7.96 (dd, 1H, J = 1.2, 8Hz); 7.87 (dd, 1H, J = 7.2, 8Hz); 7.72 (dd, 1H, J = 1.6, 7.6Hz); 7.63 -7.50 (m, 2H); 7.39-7.33 (m, 2H); 7.25 (t, 1H, J =5.6Hz); 6.95 (br s, 1H); 4.77 (d, 2H, J = 2Hz); 4.30 (br d, 1H, J = 12Hz); 4.02 (br d, 1H, J = 12Hz); 3.40-3.36 (m, 1H); 3.21-3.13 (m, 1H); 3.04-2.95 (m, 1H); 1.95-1.80 (m, 2H); 1.43-1.28 (m, 2H). LCMS Method T: retention time 1.65 min; [M+1] = 584.2; HPLC Method A1: purity 96.1%, retention time = 6.08 min.

EXAMPLE 205

1-(5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)cyclopropanecarbonitrile

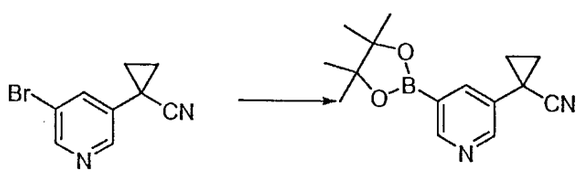


Step 1. Preparation of 1-(5-bromopyridin-3-yl)cyclopropanecarbonitrile



[00246] A suspension of 7 mL NaOH (50/50 w/w in H_2O) was charged with 2-(5-bromopyridin-3-yl)acetonitrile (from example 199: 0.36 g, 1.9 mmol). 1-Bromo-2-chloroethane (0.29 g, 2.01 mmol) was added followed by a catalytic amount of benzyl triethylammonium chloride (5 mg). The reaction mixture was stirred for 20 h at 60 °C and then poured into water. The resulting solution was extracted into ethyl acetate. The combined organic extracts were washed successively with water and brine, dried over Na_2SO_4 filtered and then concentrated to yield 1-(5-bromopyridin-3-yl)cyclopropanecarbonitrile (0.25 g, 41 %), which was used without further purification. ^{1}H NMR (400 MHz, $CDCL_3$) δ (ppm): 8.49 (d, 1H, J = 2Hz); 7.78 (d, 1H, J = 4Hz); 3.94 (q, 2H, J = 7.6 Hz); 1.69 (d, 3H, J = 7.6Hz). LCMS Method Y: retention time 1.54 min; [M+1] = 212.6.

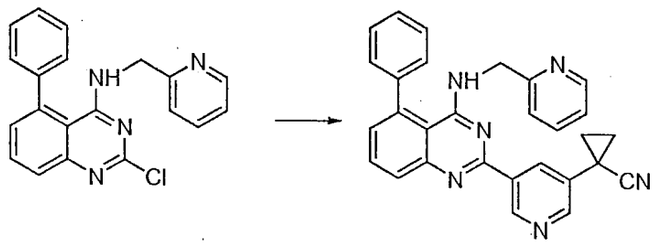
Step 2. Preparation of 1-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)cyclopropanecarbonitrile



[00247] A mixture of 1-(5-bromopyridin-3-yl)cyclopropanecarbonitrile (0.25 g, 1.1 mmol), bis(pinacolato)diboron (0.31 g, 1.2 mmol) and potassium acetate (0.44 g, 4.5 mmol) in 1,4-dioxane (8 mL) was degassed with nitrogen for 15 min. After this time, (1,1'-bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (94 mg, 0.12 mmol) was added and the reaction mixture was again degassed for 10 min with nitrogen. The reaction mixture was then heated in the microwave reactor at 120 °C for 45 min. At the conclusion of this period, the reaction mixture was filtered through celite and the filtrate was concentrated under reduced pressure to provide 1-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-

yl)cyclopropanecarbonitrile (0.28 g), which was used without further purification. LCMS Method Y: retention time 1.83 min; [M+1] = 258.8.

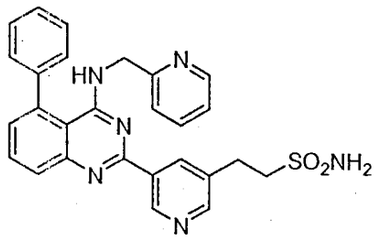
Step 3. Example 205



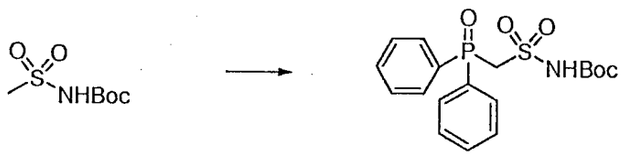
[00248] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (from example 1, step 4, 0.12 g, 0.34 mmol) in 1,4-dioxane (8 mL) and H_2O (0.55 mL) under nitrogen was added 1-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)cyclopropanecarbonitrile (0.12 g, 0.37 mmol), and potassium carbonate (0.15 g, 1.11 mmol). The reaction mixture was degassed with nitrogen for 15 min. (1,1'-Bis (diphenyphosphino) ferrocene)palladium (II) chloride dichloromethane complex (27 mg, 0.037 mmol) was added and the reaction mixture was again degassed for 10 min with nitrogen. The reaction mixture was stirred at 95 °C for 16 h, then allowed to cool to room temperature and quenched by the addition of water. The reaction mixture was transferred to a separation funnel and the aqueous layer extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (2 % methanol in DCM) to afford Example 205 (85 mg, 55 % yield) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.57 (s, 1H), 8.80 (d, 1H, J = 2Hz); 8.77 (s, 1H); 8.26 (d, 1H, J = 6Hz); 7.92 (dd, 1H, J = 1.2, 6.8Hz); 7.85 (t, 1H, J = 6.8Hz); 7.73 (dt, 1H, J = 1.6, 7.6Hz); 7.58-7.52 (m, 5H); 7.34-7.32 (m, 2H); 7.24 (t, 1H, 7.2Hz); 6.86 (t, 1H, J = 4Hz); 4.75 (d, 2H, J = 4.4Hz); 1.90 (dd, 2H, J = 4.8, 8Hz); 1.90 (dd, 2H, J = 4.8, 8Hz). LCMS Method V: retention time 1.78 min, [M+1] = 455.2; HPLC Method A1: purity 97.7 %, retention time = 7.75 min.

EXAMPLE 206

2-(5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)ethanesulfonamide

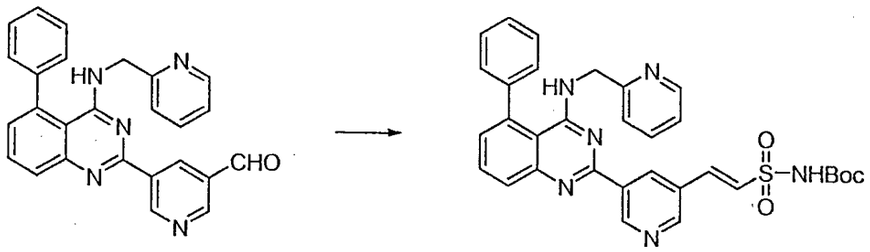


Step 1. Preparation of tert-butyl(diphenylphosphoryl)methylsulfonylcarbamate



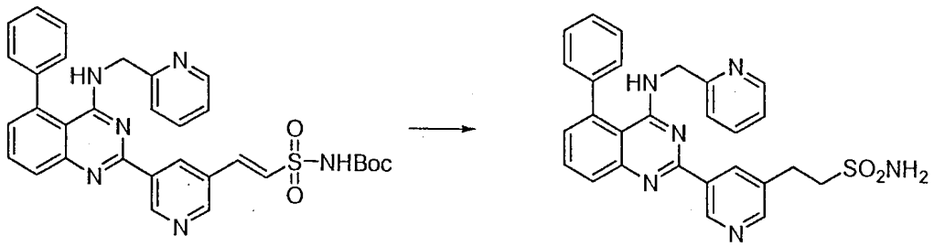
[00249] To a solution of tert-butyl methylsulfonylcarbamate (2 g, 10 mmol) in THF (25 mL) at -78 °C was added LDA (2 M in THF, 15.4 mL, 30.7 mmol). Upon completion of addition, the reaction mixture stirred for 10 min and then diphenylphosphinic chloride (2.42 g, 10.2 mmol) was added drop wise to the reaction at -78 °C. After 90 min, water (100 mL) was added and the reaction mixture was diluted with ethyl acetate (250 mL). The aqueous layer was adjusted to pH 5 with 5% aqueous HCl. The white precipitate that formed was filtered and the solid dried in vacuo to give tert-butyl(diphenylphosphoryl)methylsulfonylcarbamate (2.9 g, 72 % yield) as a white solid.

Step 2. Preparation of (E)-tert-butyl 2-(5-(5-phenyl-4-(pyridin-2-ylmethylamino) quinazolin-2-yl) pyridin-3-yl) vinylsulfonylcarbamate



[00250] A solution of tert-butyl {[(diphenylphosphoryl)methyl]sulfonyl}carbamate (0.400 g, 1.01 mmol) in N,N-dimethylformamide (20 mL) was added 95% sodium hydride (0.06 g, 2 mmol) and the reaction mixture was stirred at 0 °C for 1 h. 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinaldehyde (from example 191: 0.505 g, 1.21 mmol) was added to the reaction mixture, and the resulting mixture was stirred at room temperature for 18 h. Saturated aqueous ammonium chloride solution (100 mL) was added to the reaction mixture, and the resulting mixture was extracted with ethyl acetate. The combined organic layers were washed with saturated brine, dried over anhydrous magnesium sulfate, and filtered. The filtrate was concentrated, and the resulting residue was subjected to silica gel column chromatography ($CHCl_3$-MeOH 95:5). The resulting material was crystallized from CH_2Cl_2-hexane to give the (E)-tert-butyl 2-(5-(5-phenyl-4-(pyridin-2-ylmethylamino) quinazolin-2-yl) pyridin-3-yl) vinylsulfonylcarbamate (0.450 g, 62 % yield) as a brown solid. LCMS Method Y: retention time 1.90 min; [M+1] = 595.4.

Step 3. Example 206

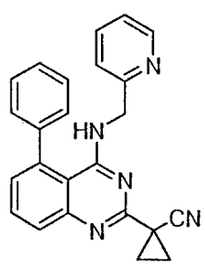


[00251] To a solution of (E)-tert-butyl 2-(5-phenyl-4-(pyridin-2-ylmethylamino) quinazolin-2-yl)vinylsulfonylcarbamate (0.210 g, 0.410 mmol) in MeOH (10 mL) was added 10 % palladium-on-carbon (20 mg) and the reaction mixture stirred at RT under a hydrogen atmosphere for 14 h. The reaction mixture was filtered and. the filtrate was concentrated under reduced pressure to yield a residue. Trifluoroacetic acid (15 mL) was added to the residue and the reaction mixture was stirred at room temperature for 2 h. After this time, the reaction mixture was concentrated under reduced pressure, sodium bicarbonate solution was added, and the resulting mixture was extracted with ethyl acetate. The combined organic layers were washed with saturated brine, dried over anhydrous magnesium sulfate, and filtered. The filtrate

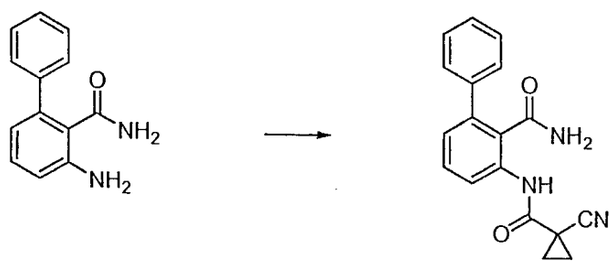
was concentrated, and the resulting residue was subjected to silica gel column chromatography ($CHCl_3$-MeOH 95:5) followed by recrystallization ($CHCl_3$-hexane) to give Example 206 (0.115 g, 65 %) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.49 (br s, 1H), 8.63 (brm, 2H), 8.27 (m, 1H), 7.91-7.82 (m, 2H), 7.74 (m, 1H), 7.59-7.55 (m, 5H),7.28-7.21 (m,1H), 6.95 (m, 2H), 6.82 (brs, 1H), 4.75 (d, J = 4.0 Hz, 2H), 3.42 (t, J=5.6Hz, 2H), 3.21 (t, J= 8Hz, 2H). LCMS Method Y: retention time 1.59 min; [M+1] = 497.2; HPLC Method A1: purity 99.6 %, retention time = 7.96 min.

EXAMPLE 207

1-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)cyclopropanecarbonitrile



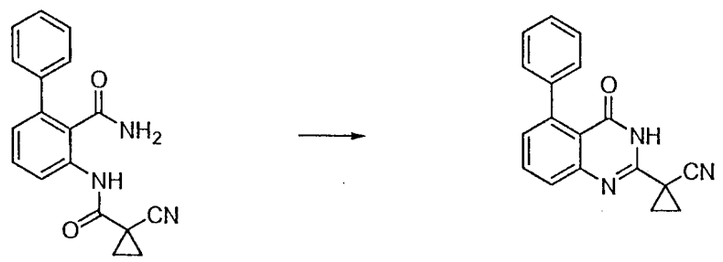
Step 1. Preparation of 3-(1-cyanocyclopropanecarboxamido)biphenyl-2-carboxamide



[00252] To a solution of 1-cyanocyclopropanecarboxylic acid (0.75 g, 7 mmol) in DCM (40 mL) was added HATU (3.5 g, 10 mmol) and DIPEA (3.4 mL, 20 mmol). After stirring at room temperature for 1 h, 3-aminobiphenyl-2-carboxamide (from example 218: 1 g, 5 mmol) was added and the reaction mixture stirred for an additional 16 h. The reaction mixture was washed with water and the organic phase

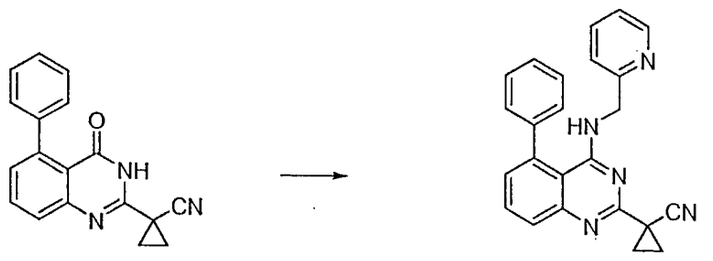
dried, filtered, concentrated under reduced pressure and purified by silica gel chromatography (60 % ethyl acetate in hexanes) to provide 3-(1-cyanocyclopropanecarboxamido)biphenyl-2-carboxamide (0.75 g,74 % yield) as a white solid. LCMS Method T: retention time 1.53 min; [M+1] = 306.2.

Step 2. Preparation of 1-(4-oxo-5-phenyl-3,4-dihydroquinazolin-2-yl)cyclopropanecarbonitrile



[00253] To a solution 3-(1-cyanocyclopropanecarboxamido)biphenyl-2-carboxamide (0.7 g, 2 mmol) in methanol was added saturated aqueous Na_2CO_3 (23 mmol) and the reaction mixture stirred at 80 °C for 30 min. The reaction mixture was concentrated under reduced pressure and the resulting residue was diluted with ethyl acetate then washed with water. The organic extracts were dried, concentrated and purified by silica gel chromatography (4 % MeOH in DCM) to yield 1-(4-oxo-5-phenyl-3,4-dihydroquinazolin-2-yl)cyclopropanecarbonitrile (0.65 g, 99 % yield) as a white solid. LCMS Method T: retention time 1.810 min; [M+1] = 288.2.

Step 3. Example 207

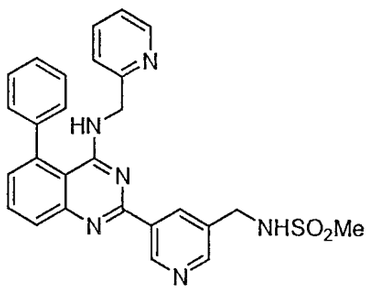


[00254] To a solution of 1-(4-oxo-5-phenyl-3,4-dihydroquinazolin-2-yl)cyclopropanecarbonitrile) (0.15 g, 0.52 mmol) in acetonitrile (3 mL) at room

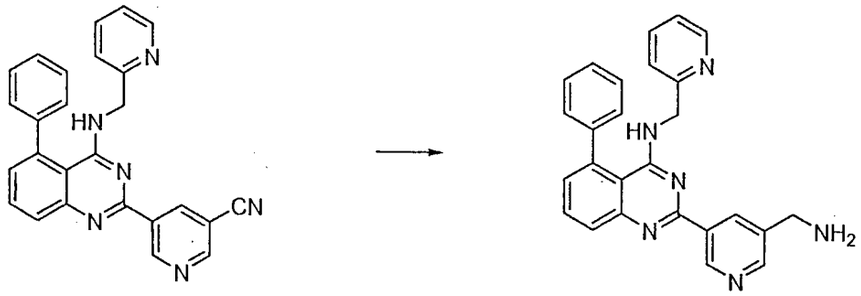
temperature was added DBU (0.25 g, 1.6 mmol) and BOP (0.3 g, 0.7 mmol) and the reaction mixture stirred for 30 min. Aminomethylpyridine (0.1 ml, 0.93 mmol) was added and the resulting reaction mixture stirred for an additional 16 h. The reaction mixture was concentrated under reduced pressure and the resulting residue was purified by silica gel column chromatography (2 % MeOH in DCM) to give Example 207 (0.05 g, 25 % yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-d6, δ): 8.23 (s, 1H); 7.82-7.62 (m, 3H); 7.60-7.46 (m, 5H); 7.21-7.28 (m, 3H); 6.76 (t, 1H, J = 4Hz); 4.52 (d, 2H, J = 4Hz); 1.78-1.74 (m, 4H). LCMS LC-MS Method V: retention time 1.80 min, [M+1] = 378.2; HPLC Method A1: purity 95.2 %, retention time = 8.75 min.

EXAMPLE 208

N-((5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)methyl)methanesulfonamide



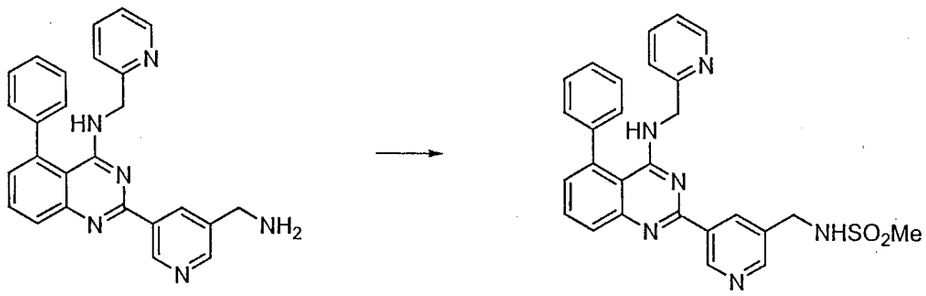
Step 1. Preparation of 2-(5-(aminomethyl)pyridin-3-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine



[00255] To a solution of 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)nicotinonitrile (from example 183: 200 mg, 0.48 mmol) in 5 % ammonia in methanol (5 mL) was added Ra-Ni (catalytic) and the resulting slurry was stirred

under hydrogen atmosphere for 16 h. After this time, the reaction mixture was filtered and the filtrate was concentrated under reduced pressure to yield 2-(5-(aminomethyl)pyridin-3-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.1 g, 50 % yield), which was used without further purification.

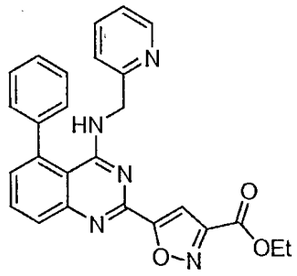
Step 2. Example 208

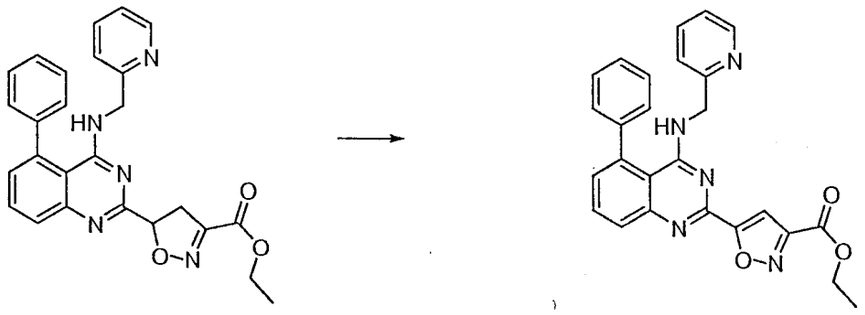


[00256] To a stirred solution of 2-(5-(aminomethyl)pyridin-3-yl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.1 g, 0.2 mmol) and TEA (0.063 mL, 0.46 mmol) in DCM (3 mL) was added methanesulfonyl chloride (0.24 mL, 0.3 mmol) drop wise at 0 °C. The reaction mixture was stirred for 1 h and then quenched by the addition of water (1 mL). The resulting solution was extracted with DCM. The combined organic extracts were washed successively with water and brine and dried, over Na_2SO_4, filtered and the filtrate concentrated under reduced pressure. The resulting residue was chromatographed on silica gel (MeOH/DCM, 2:98) to provide Example 208 (40 mg, 34 %). ^{1}H NMR (400 MHz, DMSO-d6, δ): 9.56 (s, 1H); 8.79 (s, 1H); 8.69 (s, 1H); 8.25 (d, 1H, J = 4Hz); 7.91 (dd, 1H, J = 1.6, 4Hz); 7.84 (t, 1H, J = 8Hz); 7.80-7.70 (m, 2H); 7.61-7.50 (m, 5H); 7.38-7.30 (m, 2H); 7.25 (br s, 1H); 6.85 (s, 1H); 4.76 (d, 2H, J = 4Hz); 4.35 (s, 2H); 2.98 (s, 3H). LCMS Method T: retention time 1.52 min; [M+1] = 497.2; HPLC Method A1: purity 98.5 %, retention time = 6.42 min.

EXAMPLE 209

Ethyl 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)isoxazole-3-carboxylate

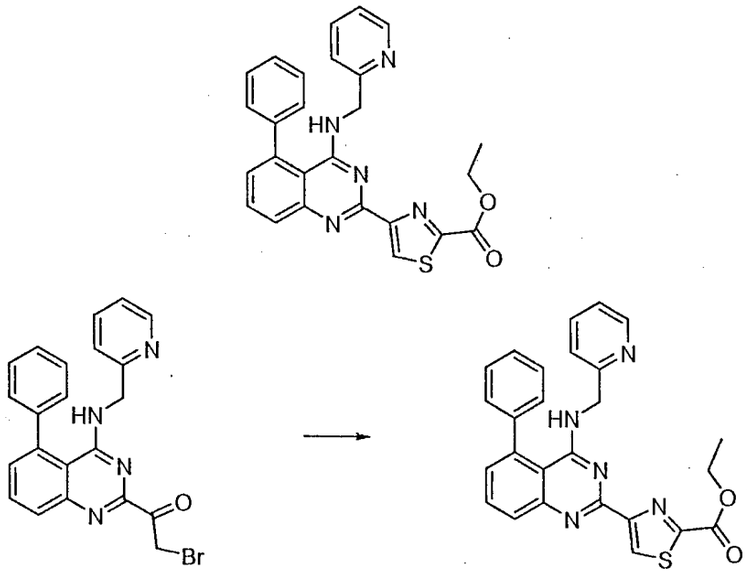




[00257] A solution of ethyl 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)-4,5-dihydroisoxazole-3-carboxylate (from example 215, see the procedure describe below, 0.30 g, 0.66 mmol), DDQ (0.06 g, 0.3 mmol) in toluene (15 mL) was heated at 75 °C for 16 h. After this time, the reaction mixture was concentrated under reduced pressure and the resulting residue was purified by ISCO chromatography (40 % ethyl acetate in hexanes) to obtain Example 209 (0.075 g, 25 % yield) as an off white solid. ^{1}H NMR (400 MHz, DMSO-d6, δ): 8.30 (s, 1H); 8.21 (s, 1H); 7.99-7.87 (m, 3H); 7.73 (dt, 1H, J = 1.6, 7.6Hz); 7.63-7.48 (m, 6H); 7.40-7.32 (m, 2H); 7.24 (dd, 1H, J = 5.6, 7.2Hz); 7.03 (br s, 1H); 4.71 (d, 2H, J = 4Hz). LCMS Method T: retention time 1.81 min; [M+1] = 423.2; HPLC Method A1: purity 99.3 %, retention time = 7.31 min.

EXAMPLE 210

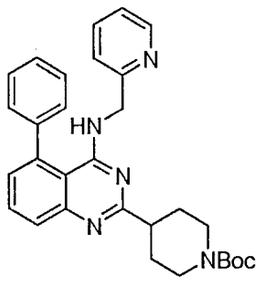
Ethyl 4-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)thiazole-2-carboxylate



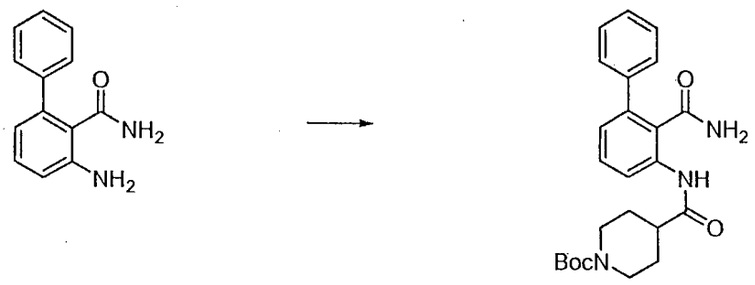
[00258] 2-Bromo-1-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)ethanone (from example 203: 0.5g, 1mmol) was dissolved in ethanol (20 mL) and ethyl thiooxamate (0.15g, 1.2mmol) was added. The reaction mixture was stirred at 70 °C for 1 hour. The ethanol was evaporated under reduced pressure and the resulting residue was dissolved in DCM (25 mL). The organic portion was washed with 10 % sodium bicarbonate solution and the aqueous layer was extracted with DCM (2 x 20 mL). The combined organic phases were dried and evaporated under reduced pressure. The resulting residue was purified by ISCO chromatography (30% ethyl acetate in hexanes) to yield Example 210 (0.13 g, 24 % yield). ^{1}H NMR (400 MHz, DMSO-d6, δ): 8.94 (s, 1H); 8.24 (d, 1H, J = 4Hz); 7.96 (d, 1H, J = 8.8Hz); 7.87 (t, 1H, J = 8Hz); 7.74 (t, 1H, J = 8Hz); 7.50-7.60 (m, 5H); 7.30-7.36 (m, 2H); 7.25 (t, 1H, J = 6Hz); 6.95 (br s, 1H); 4.75 (d, 2H, J = 4Hz); 4.47 (q, 2H, J = 7.2Hz); 1.41 (t, 3H, J = 7.2Hz). LCMS Method W: Retention time 2.243min, [M+1] = 468.2; HPLC Method A1: purity 94.4 %, retention time = 7.522 min.

EXAMPLE 211

Tert-butyl 4-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)piperidine-1-carboxylate

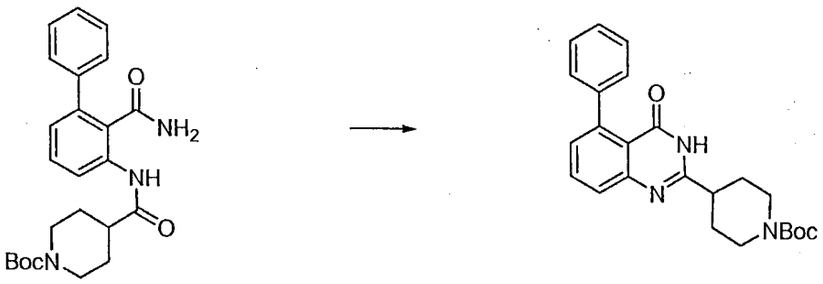


Step 1. Preparation of tert-butyl 4-(2-carbamoylbiphenyl-3-ylcarbamoyl) piperidine-1-carboxylate



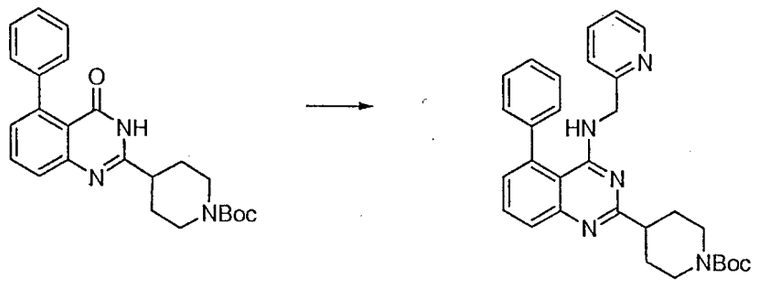
[00259] To a solution of 1-(tert-butoxycarbonyl)piperidine-4-carboxylic acid (2.4 g, 10 mmol) in DCM (40 mL) was added HATU (5.3 g, 14 mmol) and DIPEA (3.6 mL, 28 mmol) and the reaction mixture was stirred at room temperature for 1 h. 3-Aminobiphenyl-2-carboxamide (from Example 218) (1.5 g, 7.07 mmol) was added and the resulting mixture stirred for an additional 16 h. The reaction mixture was washed with water, the organic portion dried, filtered and concentrated under reduced pressure. The resulting residue was purified by ISCO chromatography (50 % ethyl acetate in hexanes) to yield tert-butyl 4-(2-carbamoylbiphenyl-3-ylcarbamoyl) piperidine-1-carboxylate (1.0g, 22 % yield) as a white solid. LCMS Method T: retention time 1.71 min; [M+1] = 423.0.

Step 2. Preparation of tert-butyl 4-(4-oxo-5-phenyl-3,4-dihydroquinazolin-2-yl)piperidine-1-carboxylate



[00260] To a solution tert-butyl 4-(2-carbamoylbiphenyl-3-ylcarbamoyl)piperidine-1-carboxylate (1.0 g, 2.4 mmol) in methanol was added NaOMe (2.6 mL, 25 % in MeOH, 12.3 mmol). The resulting reaction mixture was stirred at RT for 14 h. After this time, the reaction mixture was concentrated under reduced pressure and the resulting residue was diluted with ethyl acetate and then washed with water. The organic portion was dried, concentrated under reduced pressure to yield a residue. The residue was purified by ISCO chromatography (30% EtOAc in hexanes) to yield tert-butyl 4-(4-oxo-5-phenyl-3,4-dihydroquinazolin-2-yl)piperidine-1-carboxylate (0.60 g, 67 % yield) as a white solid. LCMS Method W: retention time 2.07 min; [M+1] = 422.2.

Step 3. Example 211

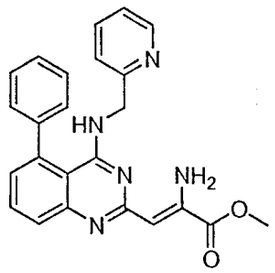


[00261] To a solution of tert-butyl 4-(4-oxo-5-phenyl-3,4-dihydroquinazolin-2-yl)piperidine-1-carboxylate (0.6 g, 1 mmol) in acetonitrile (20 mL) at room temperature was added DBU (0.45 g, 2.96 mmol) and BOP (0.98 g, 2.22 mmol). The reaction mixture was stirred for 30 min and then aminomethylpyridine (0.24 g 2.22 mmol) was added. The resulting solution was stirred for an additional 16 h. The reaction mixture was then concentrated under reduced pressure and the resulting residue was purified by silica gel chromatography (20 % EtOAc in hexanes) to

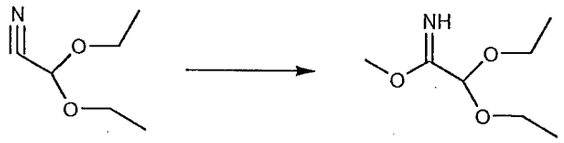
provide Example 211 (0.32 g, 45 % yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.20 (br s, 1H); 7.86-7.68 (m, 3H); 7.60-7.52 (m, 5H), 7.32-7.17 (m, 3H), 6.64 (br , 1H), 4.60 (br s, 2H), 4.04 (br d, 2H, J = 8.8 Hz), 3.03-2.79 (br m, 3H), 1.94 (br t, 2H, J = 13.6 Hz), 1.72 (dd, 2H, J = 11.2 Hz, J = 20 Hz), 1.43 (s, 9H). LCMS Method W: retention time 1.80min, [M+1] = 475.2; HPLC Method A1: purity 97.4 %, retention time = 8.08 min.

EXAMPLE 212

(Z)-methyl 2-amino-3-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)acrylate

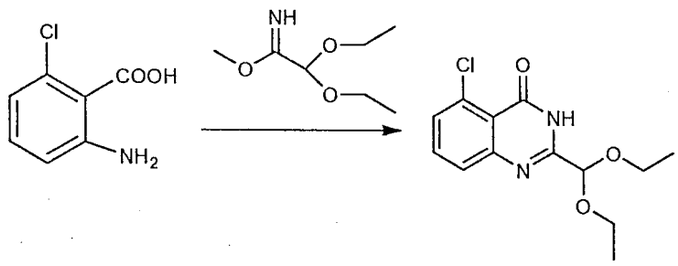


Step 1. Preparation of methyl 2,2-diethoxyacetimidate



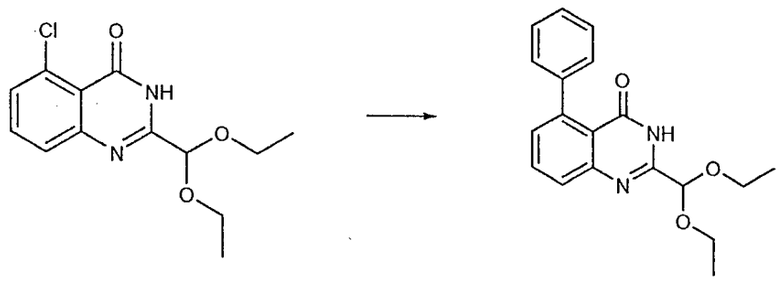
[00262] To a stirred solution of diethoxyacetonitrile (5 g, 38.75 mmol) in dry methanol (80 mL) was added 1 mL of a 20 % solution of sodium methoxide. After the addition, the reaction mixture was stirred at RT for 24 h, quenched with solid CO_2, and then concentrated. The resulting residue was diluted with water and extracted with chloroform. The organic layer was washed with brine and dried over Na_2SO_4 to yield methyl 2,2-diethoxyacetimidate (6 g, 96 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.95 (s, 1H),) , 4.82 (s, 1H), 3.66 (s, 3H), 3.49 (q , 4H, J = 7.2Hz); 1.16-1.13 (t, , 3H, J = 7.2Hz).

Step 2. Preparation of 5-chloro-2-(diethoxymethyl)quinazolin-4(3H)-one



[00263] To a stirred solution of 6-chloro anthranilic acid (6 g, 34.97 mmol) in EtOH (60 mL) under nitrogen atmosphere was added 1.5 equivalent of TEA (14 mL, 104.9 mmol). Upon completion of addition, the mixture was heated to 50 °C where it stirred for 30 min. After this time, a methyl 2,2-diethoxyacetimidate (6 g, 41.96 mmol) in ethanol solution was added through syringe and the resulting mixture was heated to reflux where it stirred for 24 h. At the conclusion of this period, the reaction mixture was cooled to RT and the volatiles were evaporated. The resulting residue was diluted with water, extracted with DCM and washed with brine solution. The crude product was purified by column chromatography (25 % ethyl acetate in hexane) to provide 5-chloro-2-(diethoxymethyl)quinazolin-4(3H)-one (7 g, 60 % yield). LCMS Method W: retention time 1.5 min; [M+1] = 283.

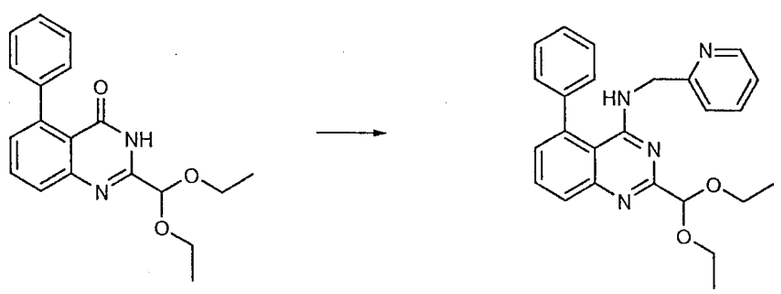
Step 3. Preparation of 2-(diethoxymethyl)-5-phenylquinozoline-4(3H)one.



[00264] To a solution of 5-chloro 2-(diethoxymethyl)quinozoline-4(3H)-one (5 g, .17.68 mmol) in a dioxane-water mixture (45:15 mL) was added phenyl boronic acid (2.8 g, 22.9 mmol) and potassium carbonate (7.32 g, 53.05 mmol). The reaction mixture was degassed with nitrogen for 30 min and then tetrakis triphenyl phosphine palladium (2.04 g, 1.76 mmol) was added. The resulting mixture was heated to reflux where it stirred for 24 h. At the conclusion of this period, the reaction mixture was

cooled to RT, concentrated and then diluted with water. The resulting mixture was filtered through celite, washed with DCM and then extracted with DCM. The organic layer was dried over Na_2SO_4, diluted with ethyl acetate, washed with water and brine, and then dried over Na_2SO_4. The crude product was purified by silica gel chromatography (25% ethyl acetate in hexane) to provide 2-(diethoxymethyl)-5-phenylquinozoline-4(3H)one (4.5 g, 78 % yield). LCMS Method V: retention time 1.62 min; [M+1] = 325.0.

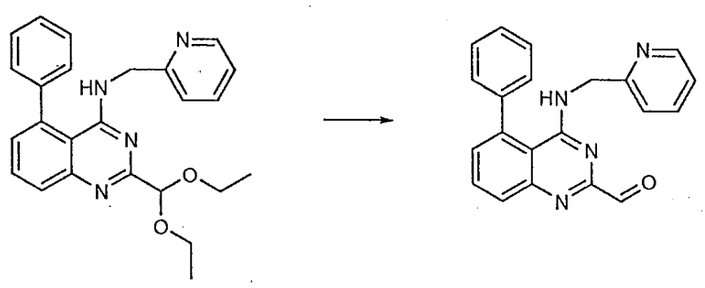
Step 4. Preparation of 2-(diethoxymethyl)-5-Phenyl-N-(pyridinyl-2-methyl)quinozoline-4-amine



[00265] To a solution of 2-(diethoxymethyl)-5-Phenylquinozoline-4(3H)one (5 g, 15.4 mmol) in acetonitrile (50 mL) under nitrogen atmosphere was added BOP reagent (10.25 g, 23.12 mmol) followed by DBU (6.3 mL,46.2 mmol). The reaction mixture was stirred at RT for an hour and then a solution of 2-aminomethyl pyridine (2.5 mL, 23.12 mmol) in acetonitrile was added. The resulting mixture was stirred at RT under nitrogen for 20 h. After this time, the solution was concentrated under reduced pressure and diluted with water. The aqueous solution was extracted with ethyl acetate and then washed with brine solution. The crude product was purified using silica gel chromatography (23 % ethyl acetate in hexane) to provide 2-(diethoxymethyl)-5-Phenyl-N-(pyridinyl-2-methyl)quinozoline-4-amine (3.3 g, 52 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.21- (s, 1H), 7.80-7.75 (m, 2H), 7.72-7.19 (m, 1H), 7.55-747 (m, 5H), 7.29-7.21 (m, 3H), 6.72 (s, 1H), 5.33 (s, 1H), 4.58 (d,

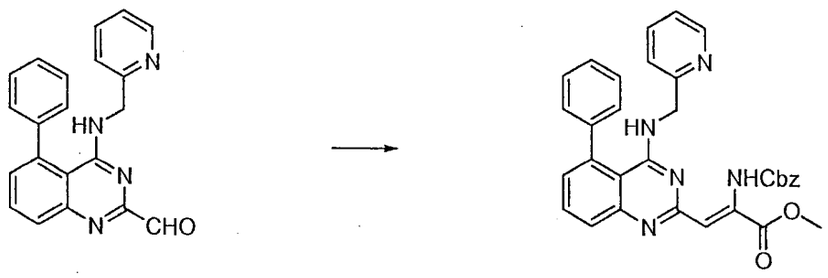
2H, J = 4Hz); 3.77-3.60 (m, 4H), 1.17-1.13 (t, 6H, J = 6.8Hz). LCMS Method V: retention time 1.69 min; [M+1] = 415.0.

Step 5. Preparation of 5-phenyl-4-(pyridin-2-ylmethylamino)quinazoline-2-carbaldehyde



[00266] To a solution of 2-(diethoxymethyl)-5-phenyl-N-(pyridinyl-2-methyl)quinozoline-4-amine (3 g, 7.24 mmol) in 1,4 dioxane (30 mL) under nitrogen atmosphere was added HCl (30 mL, 6M). The resulting mixture was heated at 90'C for 4 h. After this time, the mixture was cooled to ambient temperature and then concentrated under reduced pressure. This mixture was diluted with water, neutralized with solid Na_2CO_3 and then extracted with DCM. The organic layer was dried with sodium sulphate and evaporated under reduced pressure to yield 5-phenyl-4-(pyridin-2-ylmethylamino)quinazoline-2-carbaldehyde (1.5 g, 42 %). LCMS Method V: retention time 1.70 min; [M+1] = 340.0.

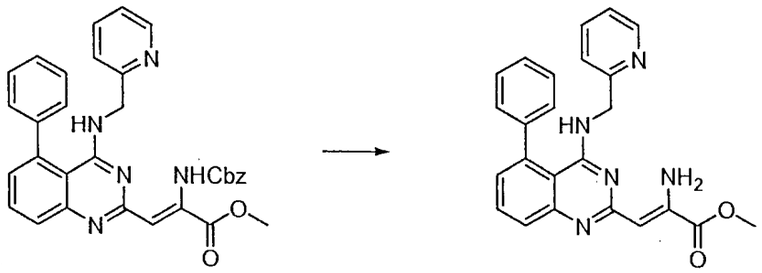
Step 6. Preparation of (Z)-methyl 2-(benzyloxycarbonylamino)-3-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)acrylate



[00267] To a solution of 5-phenyl-4-(pyridin-2-ylmethylamino)quinazoline-2-carbaldehyde (0.9 g, 3 mmol) in THF (10 mL) was added methyl 2-

benzyloxycarbonylamino-2(dimethoxyphosphinyl)acetate (0.96 g, 2.9 mmol) followed by tetramethyguanidine (0.66 mL.5.3 mmol). The resulting solution was stirred at RT for 3 h. After this time, the reaction mixture was diluted with ethyl acetate, washed successively with water and brine, dried over Na_2SO_4, filtered then and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography (30 % ethyl acetate in hexane) to yield (Z)-methyl 2-(benzyloxycarbonylamino)-3-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)acrylate (0.7 g (48 % yield). LCMS Method V: retention time 1.94 min; [M+1] = 546.0.

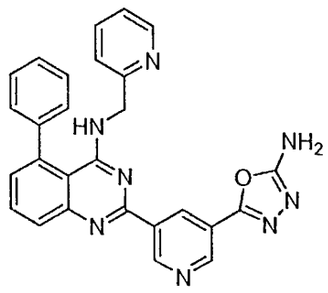
Step 7. Example 212



[00268] To a solution of (Z)-methyl 2-(benzyloxycarbonylamino)-3-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)acrylate (0.4 g, 0.7 mmol) in MeOH (7 mL) was added 10 % palladium-on-carbon (40 mg). Upon completion of addition, the reaction mixture was stirred at RT under an atmosphere of hydrogen for 20 h. After this time, the reaction mixture was filtered through celite and the filtrate was evaporated under reduced pressure. The resulting residue was purified by chromatography on silica gel (23 % ethyl acetate in hexane) to yield Example 212 (0.3 g, 88 % yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.21 (d, 1H, J = 4.4Hz); 7.72-7.68 (m, 3H), 7.54-7.45 (m, 5H), 7.25-7.21 (m, 2H), 7.14 (d, 1H, J = 6Hz); 5.97(s, 1H), 4.55 (d, 2H, J = 2.8Hz), 3.84 (s,1H). LCMS Method V: retention time 1.74 min; [M+1] = 412.0; HPLC Method A2: purity 97.7 %, retention time = 8.90 min.

EXAMPLE 213

5-(5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)-1,3,4-oxadiazol-2-amine



Step 1. Preparation of 5-bromonicotinohydrazide



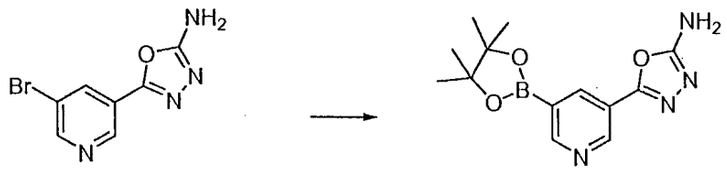
[00269] To a solution methyl 5-bromonicotinate (5 g, 23 mmol) in ethanol (40 mL) was added hydrazine hydrate (6 mL, 115 mmol). The reaction mixture was refluxed at 90 °C for 4 h. After this time, the reaction mixture was evaporated to dryness and then redissolved in ethyl acetate. The organic layer was washed with water, dried and evaporated to yield 5-bromonicotinohydrazide (3.4 g, 72 %). LCMS Method T: retention time 0.573 min; [M+1] = 216.0, 218.0.

Step 2. Preparation of 5-(5-bromopyridin-3-yl)-1,3,4-oxadiazol-2-amine



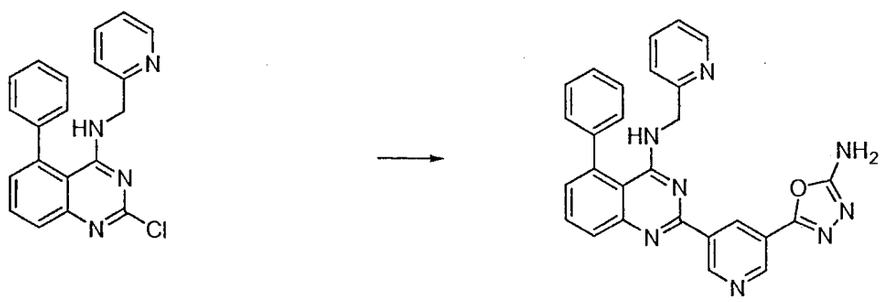
[00270] To a solution 5-bromonicotinohydrazide (2 g, 9 mmol) in dioxane (48 mL) was added sodium bicarbonate (0.78 g, 9.2 mmol) and 20 mL of water. The reaction mixture was allowed to stir for 10 min. and then cynogen bromide (1.17g, 10 mmol) was added. The resulting clear solution was allowed to stir overnight at ambient temperature. At the conclusion of this period, a pinkish precipitate was collected by filtration to yield 5-(5-bromopyridin-3-yl)-1,3,4-oxadiazol-2-amine (3.4 g, 72 % yield). LCMS Method Y: retention time 1.43 min; [M+1] = 239.0, 241.0.

Step 3. Preparation of 5-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)-1,3,4-oxadiazol-2-amine



[00271] A mixture of 5-(5-bromopyridin-3-yl)-1,3,4-oxadiazol-2-amine (0.2 g, 0.8 mmol), bis(pinacolato)diborone (0.28 g, 1.0 mmol) and potassium acetate (0.25 g, 2.5 mmol) in 1,4-dioxane (8 mL) was degassed with nitrogen for 15 min. After this time, (1,1'-bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (0.055 g 0.06 mmol) was added and the reaction mixture was again degassed for 10 min. with nitrogen. The reaction mixture was then heated in a microwave at 120 °C for 45 min. At the conclusion of this period, the reaction mixture was filtered through celite and the filtrate was concentrated under reduced pressure to provide crude 5-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)-1,3,4-oxadiazol-2-amine (0.3 g), which was used without further purification.

Step 4. Example 213

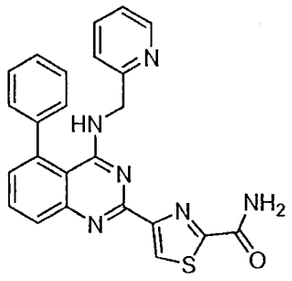


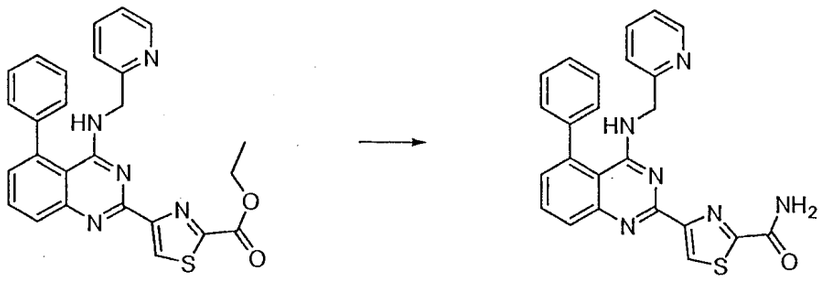
[00272] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (from example 1, step 4, 0.2 g, 0.5 mmol) in 1,4-dioxane (5 mL) and H_2O (0.55 mL) under nitrogen was added 5-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)-1,3,4-oxadiazol-2-amine (0.2 g, 0.7 mmol) and potassium carbonate (0.24 g, 1.7 mmol). The reaction mixture was degassed with nitrogen for 15 min. After this time, (1,1'-bis(diphenylphosphino)ferrocene)palladium (II) chloride

dichloromethane complex (0.047 g, 0.050 mmol) was added and the reaction mixture was again degassed for 10 min with nitrogen. At the conclusion of this period, the reaction mixture was stirred at 90 °C for 16 h, and then allowed to cool to room temperature. Once at the prescribe temperature, the reaction mixture was quenched by the addition of water. The reaction mixture was then transferred to a separation funnel and the aqueous layer was extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (5 % methanol in dichloromethane) afford Example 213 (0.067 g, 10 % yield) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.71 (s, 1H); 9.11 (s, 2H); 8.25-8.23 (m, 1H0; 7.92 (d, 1H< J = 8Hz); 7.86 (t, 1H, J = 8Hz); 7. 73 (t, 1H, J = 8Hz); 7.60-7.50 (m, 5H), 7.46 (br s, 2H); 7.37-7.31 (m, 2H); 7.22 (t, 1H, J = 4Hz); 6.93 (br s, 1H); 4.76 (d, 2H, J = 4Hz). LCMS Method W: retention time 1.80 min; [M+1] = 473.2; HPLC Method A4: purity 95.9 %, retention time = 6.11 min.

EXAMPLE 214

4-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)thiazole-2-carboxamide

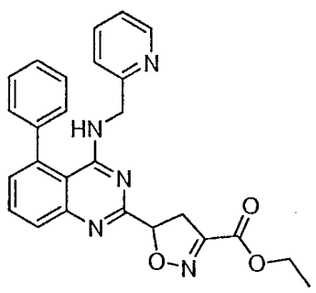




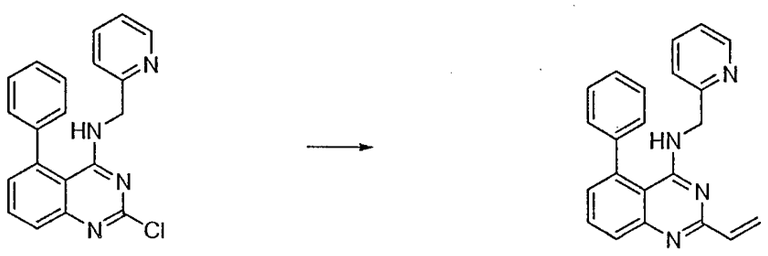
[00273] A solution of ethyl 4-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)thiazole-2-carboxylate (from example 210, 90 mg, 0.19 mmol) in NH_3 (2.0 M in MeOH, 5 mL) was stirred at RT in a sealed vessel for 30 min. The solid formed was filtered and washed with ice cooled methanol. The solid was further purified by preparative HPLC (Method S) to provide Example 214 (35 mg, 42 % yield). ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.79 (s, 1H); 8.26 (s, 1H); 8.22 (s, 1H); 7.97 (br s, 1H); 7.90-7.81 (m, 2H); 7.73 (dt, 1H, J = 2, 7.6Hz); 7.61-7.49 (m, 5H); 7.32-7.30 (m, 2H); 7.26-7.20 (m, 1H); 6.77 (t, 1H, J = 4.8Hz); 4.73 (d, 2H, J = 4.8Hz). LCMS Method W: retention time 1.85 min; [M+1] = 439.2; HPLC Method A1: purity 95.2 %, retention time = 6.26 min. Preparative HPLC Method: S.

EXAMPLE 215

1-(5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)-4,5-dihydroisoxazol-3-yl)butan-1-one



Step 1. Preparation of 5-phenyl-N-(pyridin-2-ylmethyl)-2-vinylquinazolin-4-amine



[00274] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine(0.5 g, 1.44 mmol) in 1,4-dioxane (10 mL) was added $Pd(TPP)_2Cl_2$ (0.101 g, 0.144 mmol) and tributylvinyltin (2.285 g, 7.20 mmol) under a nitrogen stream.

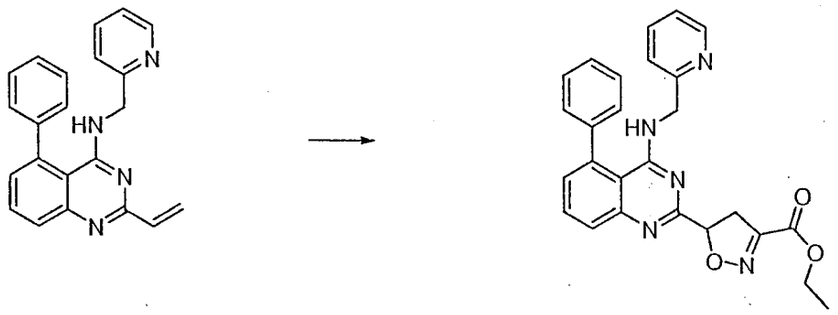
Upon completion of addition, the reaction mixture was heated to reflux at 90 °C for 16 h. After this time, the reaction mixture was allowed to cool to room temperature and then concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (20% ethyl acetate, hexane) to yield 5-phenyl-N-(pyridin-2-ylmethyl)-2-vinylquinazolin-4-amine (0.38 g, 78 % yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.22 (dd, 1H, J = 4.8Hz), 7.76 (d, 1H, J = 1.6Hz), 7.75 (s, 1H), 7.70 (dt, 1H, J = 2 Hz, 8Hz), 7.45-7.56 (m, 5H), 7.20-7.28 (m, 3H), 6.72 (dd, 1H, J = 10.4 Hz, 17.2Hz), 6.64 (t, 1H, J = 3.6Hz), 6.56 (dd, 1H, J = 1.6 Hz, 17.2 Hz), 5.67 (d, 1H, J = 10.4 Hz), 4.62 (d, 2H, J = 4.0 Hz). LCMS Method T: retention time 1.500 min; [M+1] = 339.2; HPLC Method A2: purity 98.1 %, retention time = 8.74 min.

Step 2. Preparation of (Z)-ethyl 2-chloro-2-(hydroxyimino)acetate



[00275] To a solution of glycine ester hydrochloride (2 g, 14 mmol) in 3 mL water was added conc. HCl (1.2 mL). Upon completion of addition, the resulting solution was cooled to -5 °C and then a solution of sodium nitrite (1 g, 14 mmol) in water (1.4 mL) was added. The resulting mixture was stirred at 0 °C for 10 min and then another solution of sodium nitrite (1 g, 14 mmol) in water (1.4 mL) was added. The resulting mixture was stirred at 0 °C for 45 min. At the conclusion of this period, a brine solution was added. The reaction mixture was extracted with ether, dried and evaporated under reduced pressure to yield (Z)-ethyl 2-chloro-2-(hydroxyimino)acetate (1.6 g, 76 %), was taken to the next step immediately without further purification.

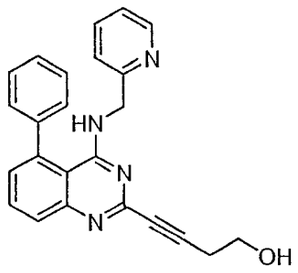
Step 3. Example 215

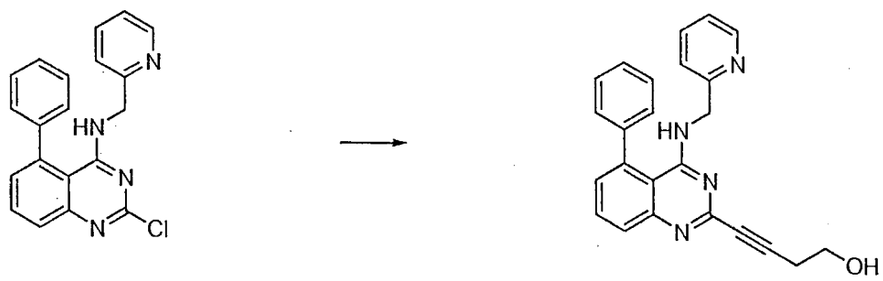


[00276] A solution of 5-phenyl-N-(pyridin-2-ylmethyl)-2-vinylquinazolin-4-amine (0.4 g, 1 mmol), (Z)-ethyl 2-chloro-2-(hydroxyimino)acetate (0.534 g, 3.54 mmol) and triethylamine (0.358 g, 3.54 mmol) in DCM (10 mL) was stirred at room temperature for 16 h. After this time, the reaction mixture was concentrated under reduced pressure to yield a residue. The residue was purified by ISCO chromatography (30 % ethyl acetate in hexane) to yield Example 215 (0.2 g, 38 % yield) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.21 (d, 1H, J = 4Hz), 7.88-7.80 (m, 2H), 7.68 (dd, 1H, J = 1.6Hz, 8.0Hz), 7.60-7.47 (m, 5H), 7.32 (dd, 1H, J = 2.4, 6.0Hz), 7.25-7.20 (m, 2H), 6.78 (br s, 1H), 5.74 (dd, 1H, J = 8, 12 Hz), 4.54 (dd, 2H, J = 4, 6.8Hz), 4.31 (q, 2H, J = 8.0 Hz), 3.73 (dd, 1H, J = 8, 17.6Hz), 3.60 (dd, 1H, J = 5.6, 17.2Hz), 1.30 (t, 3H, J = 7.2Hz). LCMS Method W: retention time 2.033 min; [M+1] = 454.4; HPLC Method A2: purity 95.1 %, retention time = 8.65 min.

EXAMPLE 216

4-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)but-3-yn-1-ol

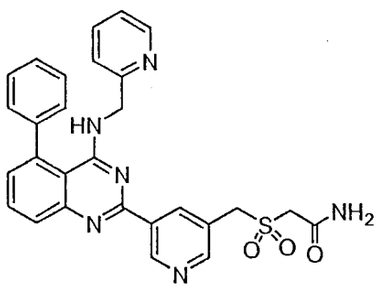




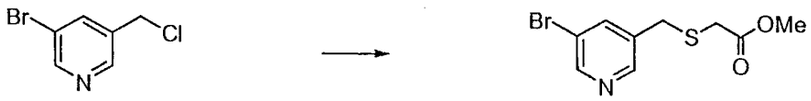
[00277] A solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (from example 1, step 4, 0.3 g, 0.9 mmol) and homopropargyl alcohol (0.07 mL, 1 mmol) in acetonitrile (10 mL) was degassed with nitrogen and then $Pd(TPP)_2Cl_2$ (0.060 g, 0.085 mmol), triethylamine (0.4 mL, 4 mmol) and CuI (0.016 g, 0.080 mmol) were added. The resulting reaction mixture was heated at 60 °C for 16 h. After this time, the reaction mixture was filtered through celite. The resulting filtrate was diluted with ethyl acetate and then washed successively with water and brine. The organic layer was dried, filtered and concentrated under reduced pressure to yield a residue. The residue was purified by silica gel chromatography (2 % methanol in hexanes) to yield Example 216 (0.15 g, 46 % yield) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.18 (br s, 1H); 7.88 (t, 1H, J = 8Hz); 7.77-7.72 (m, 2H); 7.60-7.48 (m, 5H); 7.38-7.30 (m, 3H); 7.26-7.22 (m 1H); 4.62 (d, 2H, J = 4Hz); 3.66 (t, 2H, 6.8 Hz); 2.67 (t, 2H, J = 6.8Hz). LCMS Method W: retention time 1.72 min; [M+1] = 381.2; HPLC Method A1: purity 98.5 %, retention time = 6.03 min.

EXAMPLE 217

2-((5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)pyridin-3-yl)methylsulfonyl)acetamide



Step 1. Preparation of methyl 2-((5-bromopyridin-3-yl)methylthio)acetate



[00278] To a solution of 3-bromo-5-(chloromethyl)pyridine (from example 199, (1.2 g, 5.8 mmol) in acetonitrile (15 mL) was added K_2CO_3 (0.97 g, 7.0 mmol) followed by methyl 2-mercaptoacetate (0.57 mL, 6.4 mmol). The resulting solution was stirred at room temperature for 16 h. After this time, the reaction mixture was filtered and the filtrate was diluted with ethyl acetate and washed with water. The organic portion was dried, filtered and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography (30 % ethyl acetate in hexane) to yield methyl 2-((5-bromopyridin-3-yl)methylthio)acetate (1.2 g, 80 % yield). LCMS Method Y: retention time 1.66 min; [M+1] = 276.0.

Step 2. Preparation of 2-((5-bromopyridin-3-yl)methylthio)acetamide



[00279] A solution of methyl 2-((5-bromopyridin-3-yl)methylthio)acetate (1.2 g, 4.5 mmol) in NH_3 (2.0 M in MeOH, 40 mL) was heated at 80 °C in a sealed vessel for 2 h. After this time, the reaction mixture was allowed to cool to room temperature and then the solvent was evaporated under reduced pressure. The resulting residue was recrystallized from EtOAc/hexanes to provide 2-((5-bromopyridin-3-yl)methylthio)acetamide (0.8 g, 72 % yield). LCMS Method W: retention time 1.08 min; [M+1] = 263.0.

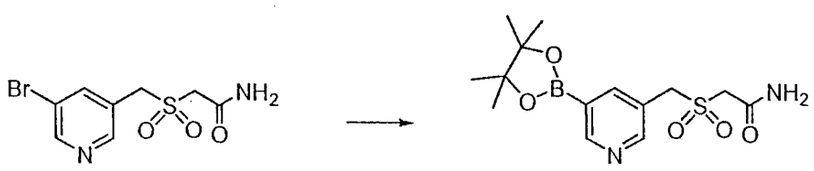
Step 3. Preparation of 2-(5-bromopyridin-3-yl)methylsulfonyl)acetamide



[00280] To a solution of 2-((5-bromopyridin-3-yl)methylthio)acetamide (0.8 g, 3.0 mmol) in MeOH:H_2O (30:10 mL) was added oxone® (2.5 g, 3.9 mmol). The

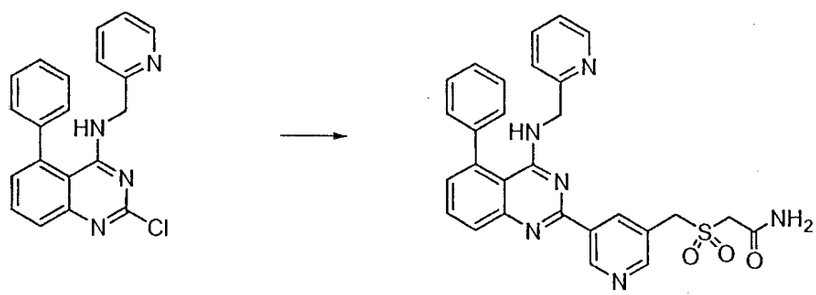
resulting reaction mixture was stirred at room temperature for 2 h. After this time, the solvent was evaporated and the resulting residue was dissolved in EtOAc and washed with water. The organic portion was concentrated to provide 2-(5-bromopyridin-3-yl)methylsulfonyl)acetamide (0.6 g, 67 %). LCMS Method T: retention time 0.68 min; [M+1] = 293.

Step 4. Preparation of 2-((5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)methylsulfonyl)acetamide



[00281] A mixture of 2-(5-bromopyridin-3-yl)methylsulfonyl)acetamide (10.3 g, 1.00 mmol), bis(pinacolato)diboron (0.337 g, 1.30 mmol) and potassium acetate (0.3 g, 3.0 mmol) in 1,4-dioxane (10 mL) was degassed with nitrogen for 15 min. After this time, (1,1'-bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (0.066 mg, 0.08 mmol) was added and the reaction mixture was again degassed for 10 min. with nitrogen. The reaction mixture was heated in the microwave reactor at 120 °C for 45 min. At the conclusion of this period, the reaction mixture was filtered through celite and the filtrate was concentrated under reduced pressure to provide 2-((5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)methylsulfonyl)acetamide (440 mg) as a brown solid, which was used without further purification.

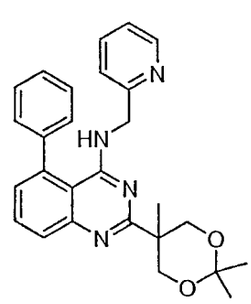
Step 5. Example 217



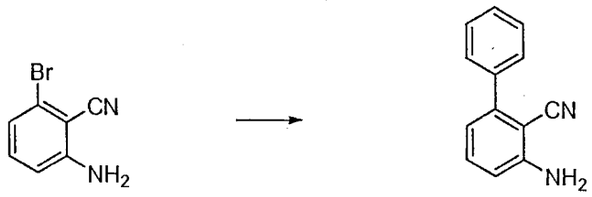
[00282] To a solution of 2-chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (from example 1, step 4, 0.3 g, 0.9 mmol) in 1,4-dioxane (10 mL) and H_2O (2 mL) under nitrogen was added 2-((5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)methylsulfonyl)acetamide (0.3 g, 0.9 mmol), and potassium carbonate (0.36 g, 2.6 mmol). The reaction mixture was degassed with nitrogen for 15 min and then (1,1'-bis(diphenylphosphino)ferrocene)palladium (II) chloride dichloromethane complex (0.07 g, 0.08 mmol) was added. The reaction mixture was again degassed for 10 min with nitrogen and then stirred at 90°C for 16 h. At the conclusion of this period, the reaction mixture was allowed to cool to room temperature and then quenched by the addition of water. The reaction mixture was transferred to a separation funnel and the aqueous layer was extracted with ethyl acetate. The combined organic portions were washed with water and saturated NaCl, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting concentrate was purified by preparative TLC (5 % methanol in dichloromethane) to provide Example 217 (100 mg, 22 % yield) as an off white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.62 (s, 1H); 9.84 (s, 1H); 8.84 (s, 1H); 8.23 (br s, 1H); 7.92-7.88 (m, 1H); 7.85 (t, 2H, J = 4Hz); 7.72 (t, 1H, J = 8Hz); 7.60-7.50 (m, 6H); 7.40-7.28 (m, 2H); 7.22 (t, 1H, J = 8Hz); 6.85 (br s, 1H); 4.85 (s, 2H); 4.73 (d, 2H, J = 4HZ); 4.06 (s, 2H). LCMS Method W: retention time 1.70 min; [M+1] = 525.2; HPLC Method A2: purity 99.5 %, retention time = 5.91 min.

EXAMPLE 218

5-Phenyl-N-(pyridin-2-ylmethyl)-2-(2,2,5-trimethyl-1,3-dioxan-5-yl)quinazolin-4-amine

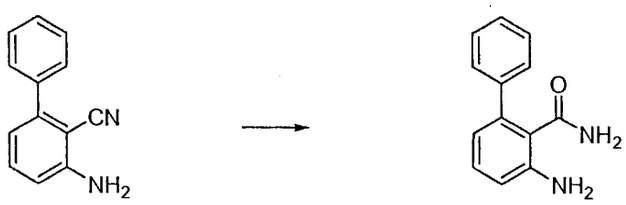


Step 1. Preparation of 3-aminobiphenyl-2-carbonitrile



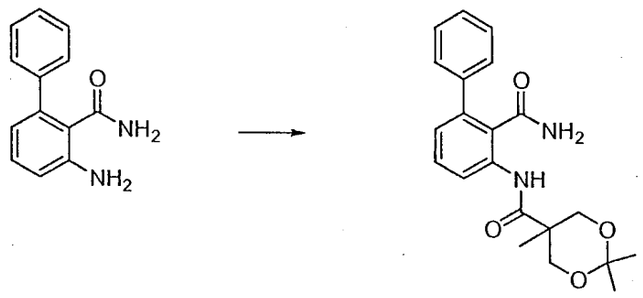
[00283] To a solution of 2-amino-6-bromobenzonitrile (5 g, 0.025 mmol) in toluene (70 mL) was added KOAc (5g, 0.05 mmol), phenylboronic acid (4.27 g, 0.035 mmol) and cat. $Pd(TPP)_2Cl_2$. The reaction mixture was heated to 115 °C for 16 h. After this time, the reaction mixture was filtered and the volatiles were evaporated to yield as residue. The residue was purified by column chromatography (1% EtOAc in hexanes) to provide 3-aminobiphenyl-2-carbonitrile (3.2 g, 65 % yield) as light yellow solid. LCMS Method Z: retention time 3.65 min; [M+] = 195.2.

Step 2. Preparation of 3-aminobiphenyl-2-carboxamide



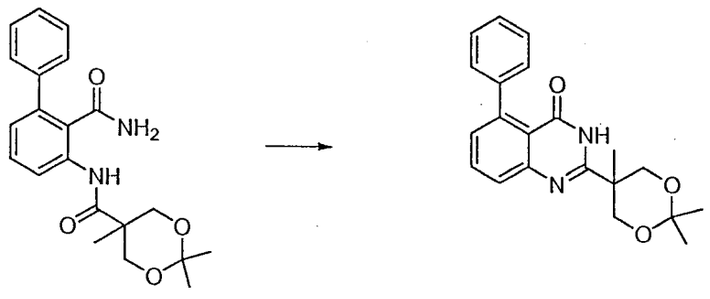
[00284] A solution of 3-aminobiphenyl-2-carbonitrile (4 g, 20 mmol) in ethanol (20 mL) and aqueous NaOH (8 g, 200 mmol) was heated at 100 °C in the microwave reactor for 1 h 30 min. After this time, the ethanol was evaporated under reduced pressure and the resulting residue was extracted with ethyl acetate. The organic extracts were concentrated under reduced pressure to yield a residue. The residue was purified by silica gel chromatography (50 % EtOAc in hexane) to give 3-aminobiphenyl-2-carboxamide (3.1 g, 72 % yield) as a brown solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.40-7.30 (m, 5H), 7.15 (br s, 1H), 7.11 (t, 1H, J = 8Hz), 6.72 (dd, 1H, J = 0.8, 8 Hz), 6.52 (dd, 1H, J =0.8, 8 Hz), 5.13 (s, 1H). LCMS Method W: retention time 1.28 min; [M+1] = 213.0.

Step 3. Preparation of N-(2-carbamoylbiphenyl-3-yl)-2,2,5-trimethyl-1,3-dioxane-5-carboxamide



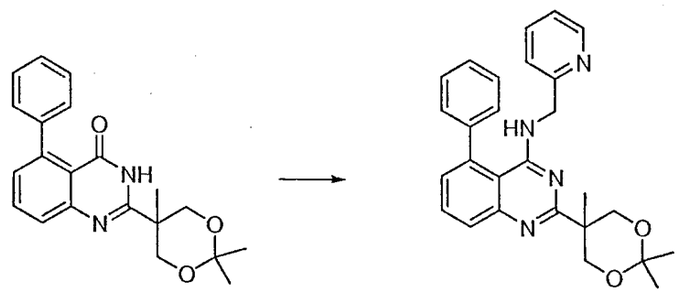
[00285] To a solution of the commercially available 2,2,5-trimethyl-1,3-dioxane-5-carboxylic acid (0.6 g, 4 mmol) in DCM (30 mL) was added HATU (1.8 g, 4.7 mmol) and DIPEA (1.6 mL, 23.5 mmol). The reaction mixture was stirred at room temperature for 1 h. After this time, 3-aminobiphenyl-2-carboxamide (0.6 g, 2.35 mmol) was added and the resulting solution was stirred for 16 h. At the conclusion of this period, the reaction mixture was washed with water, dried, filtered and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography (25% ethyl acetate in hexanes) to yield N-(2-carbamoylbiphenyl-3-yl)-2,2,5-trimethyl-1,3-dioxane-5-carboxamide (0.25 g, 24 % yield) as a white solid. LCMS Method Y: retention time 1.69 min; [M+1] = 367.2.

Step 4. Preparation of 5-phenyl-2-(2,2,5-trimethyl-1,3-dioxan-5-yl)quinazolin-4(3H)-one



[00286] To a solution N-(2-carbamoylbiphenyl-3-yl)-2,2,5-trimethyl-1,3-dioxane-5-carboxamide (0.23 g, 0.62 mmol) in methanol was added NaOMe (0.25 mL, 25 % in MeOH, 1.2 mmol) and the reaction mixture stirred at 50 °C for 1 h. After this time, the reaction mixture was concentrated and the resulting residue was diluted with ethyl acetate then washed with water. The organic portion was dried and concentrated under reduced pressure to yield a residue. The residue was purified by silica gel chromatography (30 % ethyl acetate in hexanes) to yield pure 5-phenyl-2-(2,2,5-trimethyl-1,3-dioxan-5-yl)quinazolin-4(3H)-one (0.2 g, 91 % yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 11.49 (br s, 1H), 7.77 (t, 1H, J = 8Hz), 7.64 (d, 1H, J = 8Hz), 7.36-7.28 (m, 5H), 7.21 (d, 1H, J = 8Hz), 4.27 (d, 2H, J = 12Hz), 3.91 (d, 2H, J = 12Hz), 1.40 (s, 3H), 1.35 (d, 6H, 10.2Hz). LCMS Method W: retention time 2.01 min; [M+1] = 351.

Step 5. Example 218

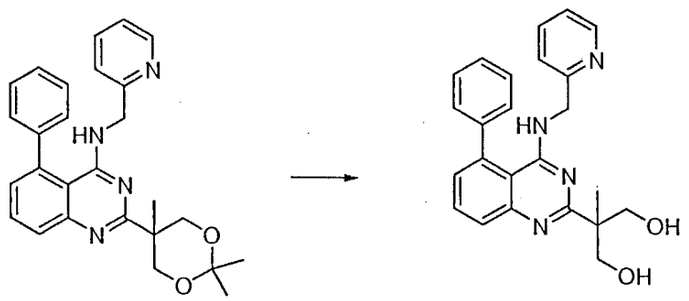


[00287] To a solution of 5-phenyl-2-(2,2,5-trimethyl-1,3-dioxan-5-yl)quinazolin-4(3H)-one (0.22 g, 0.62 mmol) in acetonitrile (10 mL) at room temperature was added DBU (0.24 g, 1.57 mmol) and BOP reagent (0.36 g, 0.81 mmol). The reaction mixture was stirred for 30 min and then aminomethylpyridine (0.11 mL, 1.1 mmol) was added. The resulting solution was stirred for 16 h. After this time, the reaction mixture was concentrated under reduced pressure and the resulting residue was purified by silica gel chromatography (30 % EtOAc in hexanes) to give Example 219 (0.18 g, 67 % yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-d6, δ): 8.26 (br s, 1H); 7.80-7.69 (m, 3H); 7.59-7.45 (m, 5H); 7.27-7.20 (m, 3H); 6.53 (br s, 1H); 4.55 (d, 2H, J = 4Hz); 4.31 (d, 2H, J = 7.6Hz); 3.79 (d, 2H, J = 7.6Hz); 1.38 (d, 6H, J =

4.8Hz); 1.33 (s, 3H). LCMS Method W: retention time 2.37 min, [M+1] = 441; HPLC Method A1: purity 96.7 %, retention time = 6.87 min.

EXAMPLE 219

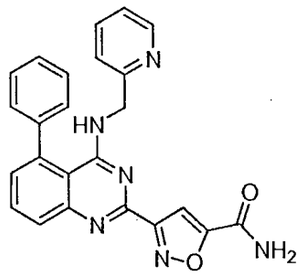
2-Methyl-2-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)propane-1,3-diol.



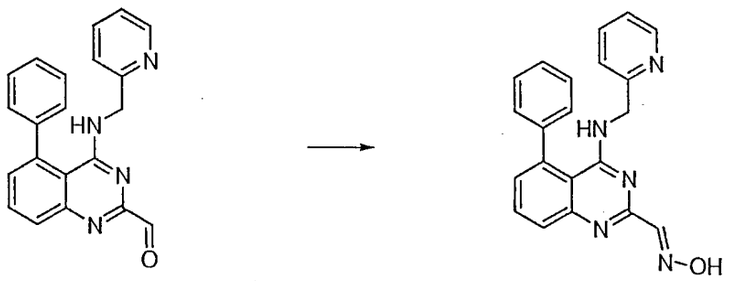
[00288] 5-Phenyl-N-(pyridin-2-ylmethyl)-2-(2,2,5-trimethyl-1,3-dioxan-5-yl)quinazolin-4-amine (from example 218, 0.1 g, 0.23 mmol) was dissolved in ether (2 mL). Upon dissolution, M HCl in ether (5 mL) was added and the resulting mixture was stirred at RT for 4 h. After this time, the resulting solution was neutralized with sat. $NaHCO_3$ solution. The ether was evaporated and the aqueous layer residue was extracted in ethyl acetate. The organic extracts were dried and evaporated. The resulting residue was purified by silica gel column chromatography (2 % methanol in dichloromethane) to yield Example 219 (56 mg, 62 % yield). ^1H NMR (400 MHz, DMSO-d6, δ): 8.24 (br s, 1H); 7.80-7.63 (m, 3H); 7.54-7.44 (m, 5H); 7.24-7.20 (m, 3H); 6.56 (br s, 1H); 4.57 (s, 2H), 4.56 (d, 2H, J = 6 Hz); 3.77 (d, 4H, J = 6 Hz); 1.23 (s, 3H). LCMS Method W: retention time 1.77 min, [M+1] = 401; HPLC Method A1: purity 95.14 %, retention time = 9.78 min.

EXAMPLE 220

3-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)isoxazole-5-carboxamide

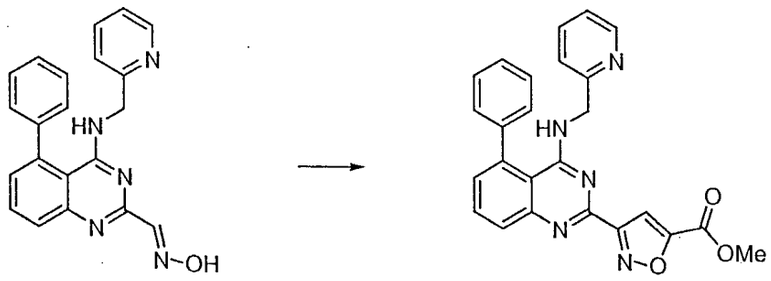


Step 1. Preparation of (E)-5-phenyl-4-(pyridin-2-ylmethylamino)quinazoline-2-carbaldehyde



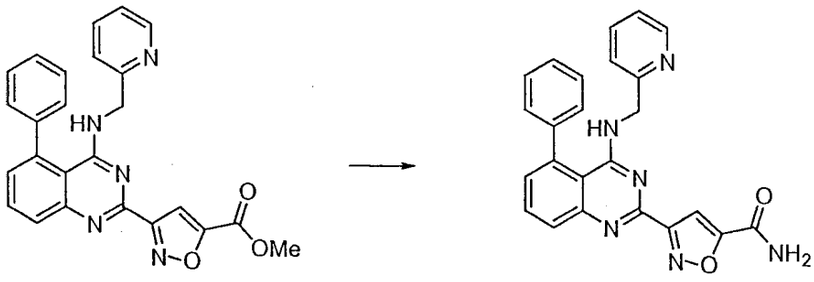
[00289] A solution of 5-phenyl-4-(pyridin-2-ylmethylamino)quinazoline-2-carbaldehyde (from example 212, 0.62 g, 1.8 mmol), hydroxylamine hydrochloride (0.19 g, 2.8 mmol) and sodium acetate (0.30 g, 3.7 mmol) in water (10 mL) was heated at 100 °C for 30 min. After this time, the reaction mixture was allowed to cool to RT and then extracted with DCM (2 x 50 mL). The combined organic portions were concentrated under reduced pressure and the resulting residue was purified by silica gel chromatography (0.8 % MeOH in DCM) to provide (E)-5-phenyl-4-(pyridin-2-ylmethylamino)quinazoline-2-carbaldehyde (0.4 g, 60 % yield) as a yellow solid. LCMS Method W: retention time 1.703 min, [M+1] = 356.2.

Step 2. Preparation of methyl 3-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)isoxazole-5-carboxylate



[00290] To a solution of (E)-5-phenyl-4-(pyridin-2-ylmethylamino)quinazoline-2-carbaldehyde oxime (0.32 g, 0.90 mmol) and methylpropriolate (0.227 g, 2.70 mmol) in acetonitrile was added CrO_2 (magtrieve) (0.75 g, 9.0 mmol). The reaction mixture was heated at 80 °C for 2 h. After this time, the reaction mixture was allowed to cool to RT. Once at the prescribed temperature, the reaction mixture was diluted with ethyl acetate and filtered through celite. The filtrate was evaporated under reduced pressure and the resulting residue was purified by silica gel chromatography (1.5 % MeOH in DCM) to provide methyl 3-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)isoxazole-5-carboxylate (120 mg, 30 % yield) as an off white solid. LCMS Method W: retention time 2.185 min, [M+1] = 438.2.

Step 3. Example 220

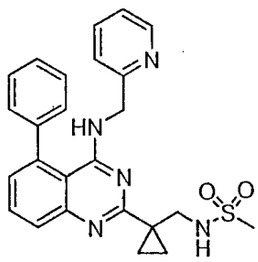


[00291] A solution of 3-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)isoxazole-5-carboxylate (90 mg, 0.199 mmol) in NH_3 (2.0 M in MeOH, 5 mL) was heated at 60 °C in a sealed vessel for 8 h. After this time, the reaction mixture was allowed to cool to room temperature and the solvent was evaporated under reduced pressure. The resulting residue was purified by preparative HPLC (Method S) to provide Example 220 (35 mg, 42 % yield). ^{1}H NMR (400 MHz, DMSO-d6, δ): 8.45

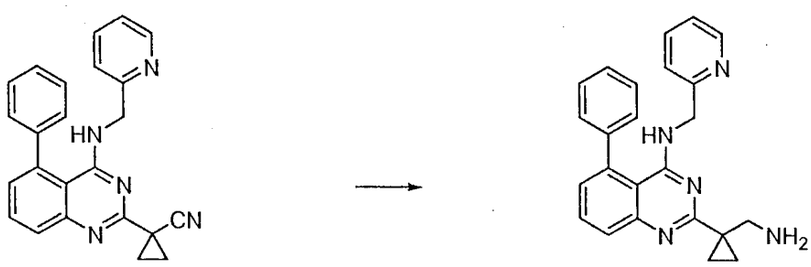
(s, 1H); 8.21 (s, 1H); 8.05 (s, 1H); 7.92-7.85 (m, 2H); 7.73 (dt, 1H, *J* = 1.2, 7.6Hz); 7.67 (s, 1H); 7.60-7.49 (m, 5H); 7.40-7.30 (m, 3H); 7.24 (t, 1H, *J* = 5.6Hz); 7.00 (t, 1H, *J* = 4Hz); 4.69 (d, 2H, *J* = 4Hz). LCMS Method W: Retention time 1.74min, [M+1] = 423.2; HPLC Method A1: purity 99.3 %, retention time = 6.78 min.

EXAMPLE 221

N-((1-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)cyclopropyl)methyl)methanesulfonamide

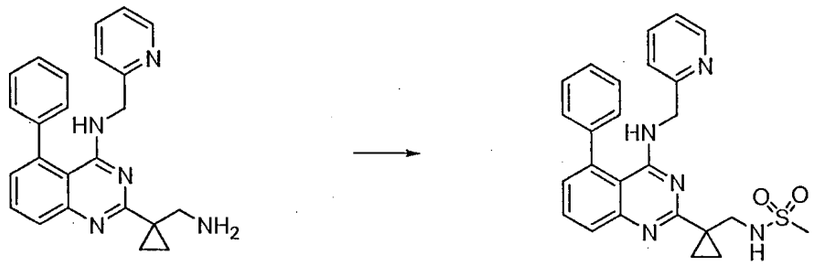


Step 1. Preparation of 2-(1-(aminomethyl)cyclopropyl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine



[00292] To a solution of 1-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)cyclopropanecarbonitrile (Example 207, 0.6 g, 2 mmol) in 7 M ammonia methanol (10 mL) was added Ra-Ni (200 mg). The resulting slurry was stirred under hydrogen atmosphere for 16 h. After this time, the reaction mixture was filtered and filtrate was concentrated under reduced pressure to yield 2-(1-(aminomethyl)cyclopropyl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (380 mg, 63 % yield), which was used without further purification.

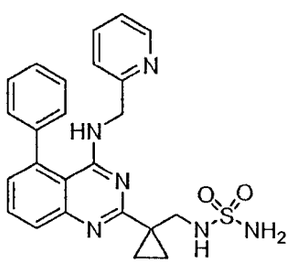
Step 2. Example 221

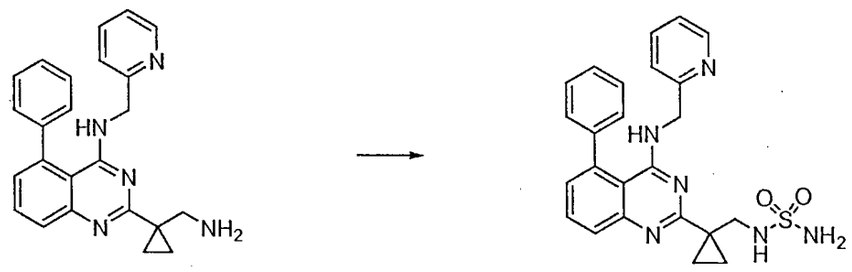


[00293] To a stirred solution of 2-(1-(aminomethyl)cyclopropyl)-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine (60 mg, 0.16 mmol) and TEA (0.05 ml, 0.43 mmol) in DCM (5 mL) was added methanesulfonyl chloride (0.015 mL, 0.18 mmol) dropwise at 0 °C. The reaction mixture was allowed to reach RT where it stirred for 2 h. After this time, the reaction mixture was quenched with water and then extracted with EtOAc. The combined organic extracts were washed successively with water and brine, dried, and filtered. The filtrate was concentrated under reduced pressure to yield a residue. The residue was purified by silica gel chromatography (15% EtOAc, hexane) to provide Example 221 (25 mg, 36 % yield) as a solid. ^{1}H NMR (400 MHz, DMSO-d6, δ): 8.25 (d, 1H, J = 4.4Hz); 7.80-7.68 (m, 3H); 7.60-7.43 (m, 5H); 7.27-7.15 (m, 3H); 6.95 (t, 1H, J = 6Hz), 6.53 (s, 1H), 4.54 (d, 2H, J = 4Hz), 3.54 (d, 2H, J = 6.4Hz), 2.99 (s, 3H), 1.30 (d, 2H, J = 2.4Hz, 1.01 (d, 2H, J = 2.4Hz). LCMS Method V: retention time 1.77 min, [M+1] = 460.0; HPLC Method A1: purity 99.1 %, retention time = 6.29 min.

EXAMPLE 222

N-((1-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)cyclopropyl)methyl)sulfamide

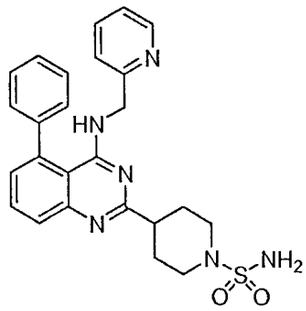




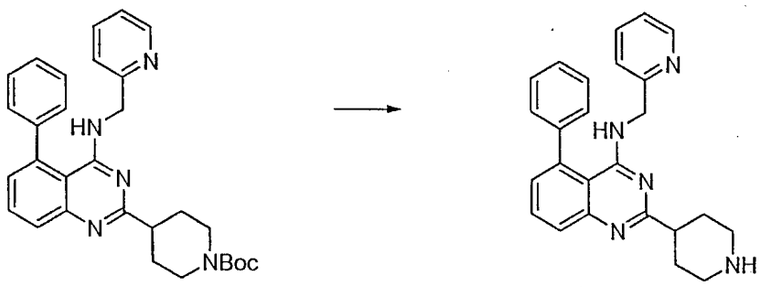
[00294] To a solution chlorosulfonylisocyanate (0.03 mL, 0.2 mmol) in DCM (1 mL) was added t-BuOH (0.16 mL, 0.21 mmol) at 0 °C. The reaction mixture was stirred for 10 min. After this time, the reaction mixture was added to a mixture of 2-(1-(aminomethyl)cyclopropyl)-5-phenyl-N-(pyridin-2-ylmethyl) quinazolin-4-amine (from example 221, 80 mg, 0.21 mmol) and TEA (0.043 ml, 0.42 mmol) in DCM at 0 °C. The resulting reaction mixture was stirred for an additional 3 h at room temperature. At the conclusion of this period, the reaction mixture was quenched with water (15 mL) and then extracted with DCM. The combined organic extracts were washed successively with water and brine, dried with Na_2SO_4, filtered and concentrated under reduced pressure to yield a residue. TFA (2 mL) was added to the residue and the resulting reaction mixture was stirred for 2 h and then concentrated in vacuo. The resulting residue was diluted with EtOAc (20 mL) and washed successively with saturated $NaHCO_3$ and brine, dried over Na_2SO_4 filtered and the solvent was removed under reduced pressure. The resulting residue was purified by silica gel chromatography (5 % MeOH in DCM) to yield Example 222 (25 mg, 27 % yield). ^{1}H NMR (400 MHz, DMSO-d6, δ): 8.24 (dd, 1H, J= 1.2Hz, 7.2Hz); 7.67-7.80 (m, 3H); 7.58-7.43 (m, 5H); 7.28-7.16 (m, 3H); 6.63 (s, 2H), 6.53 (br s, 1H), 6.48-6.43 (m, 1H), 4.52(d, 2H, J= 4Hz), 3.45 (d, 2H, J = 7.6Hz), 1.28 (d, 2H, J= 4Hz), 1.02 (d, 2H, J= 4Hz). LCMS Method W: retention time 1.93 min, [M+1] = 461.2; HPLC Method A1: purity 96.5 %, retention time = 5.91 min.

EXAMPLE 223

4-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)piperidine-1-sulfonamide

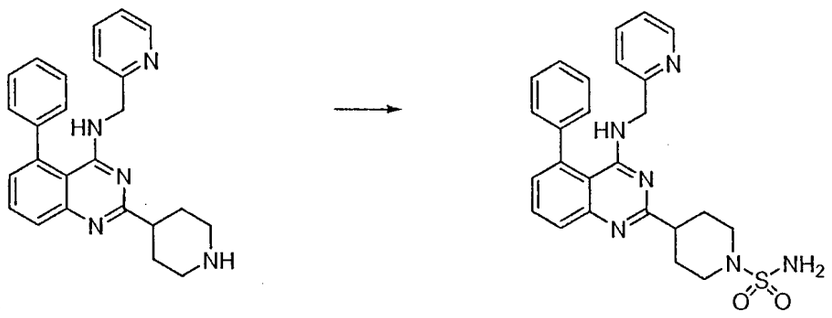


Step 1. Preparation of 5-phenyl-2-(piperidin-4-yl)-N-(pyridin-2-ylmethyl)quinazolin-4-amine



[00295] Tert-butyl 4-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)piperidine-1-carboxylate (Example 211, 0.2 g 0.4 mmol) was dissolved in 10 mL HCl (2 M in ether). The reaction mixture stirred at RT for 16 h. After this time, the solvent was removed under reduced pressure. The resulting residue was neutralized with sat. $NaHCO_3$ and the aqueous phase was extracted into DCM. The combined organic extracts were concentrated under reduced pressure and the resulting residue was purified by recrystallization with EtOAc to yield 5-phenyl-2-(piperidin-4-yl)-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.13 g, 76 % yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.21 (d, 1H, J = 4.0 Hz), 7.77-7.66 (m, 3H), 7.58-7.40 (m, 5H), 7.30-7.15 (m, 3H), 6.57 (br s, 1H), 4.56 (d, 2H, J = 4.0 Hz), 3.05 (d, 2H, J = 12.0 Hz), 2.80-2.70 (m, 1H), 2.60 (t, 2H, J = 8.0 Hz), 1.95-1.80 (m, 2H), 1.80-1.65 (m, 2H). LCMS Method W: retention time 1.43 min, [M+1] = 396.2; HPLC Method A1: purity 96.4 %, retention time = 9.00 min.

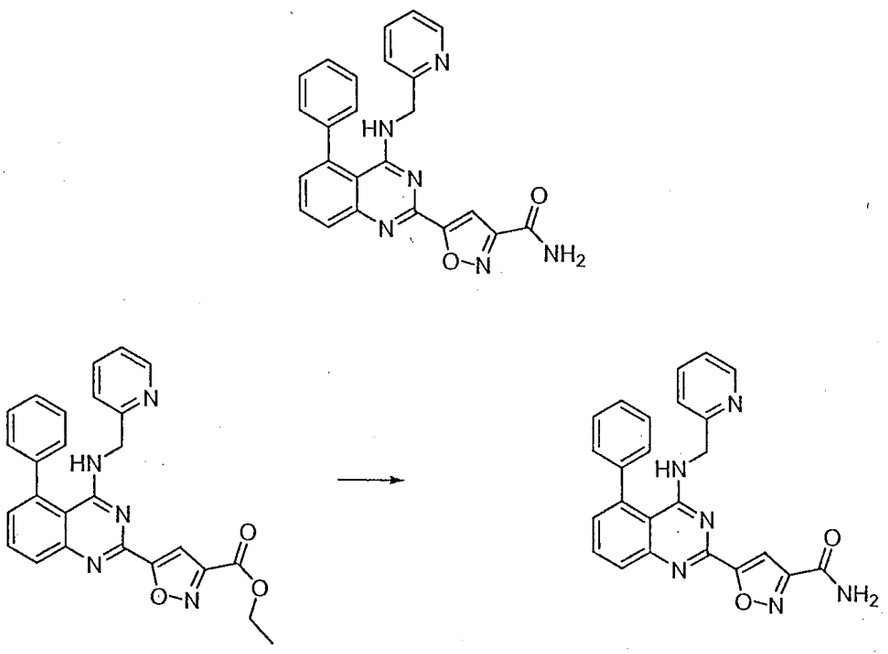
Step 2. Example 223



[00296] To a solution chlorosulfonylisocyanate (0.035 g, 0.25 mmol) in DCM (5 mL) was added t-BuOH (0.019 g, 0.25 mmol) at RT. The reaction mixture was stirred for 10 min and then TEA (0.038 g, 0.37 mmol) was added followed by 5-phenyl-2-(piperidin-4-yl)-N-(pyridin-2-ylmethyl)quinazolin-4-amine (0.1 g, 0.3 mmol) in DCM. The resulting reaction mixture was stirred for an additional 3 h. After this time, the reaction mixture was diluted with water and then extracted in EtOAc. The combined organic extracts were dried and concentrated under reduced pressure to yield a residue. The residue was treated with etherial HCl (4 ml, 2 M solution). The resulting solution was concentrated under reduced pressure and the resulting residue was purified by recrystallization using EtOAc to yield Example 223 (0.038 g, 32 % yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.20 (s, 1H), 7.80-7.66 (m, 3H), 7.58-7.43 (m, 5H), 7.27 (d, 1H, J = 8.0Hz), 7.24-7.18 (m, 2H), 6.73 (br s, 2H),6.65 (t, 1H, J = 4.0 Hz), 4.58 (d, 1H, J = 8.0 Hz), 3.55 (d, 2H, J = 12.0 Hz), 2.81-2.64 (m, 3H), 2.10-2.04 (m, 2H), 2.00-1.86 (m, 2H). LCMS Method V: retention time 1.62 min, [M+1] = 475; HPLC Method A1: purity 98.7 %, retention time = 6.26 min.

EXAMPLE 224

5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)isoxazole-3-carboxamide

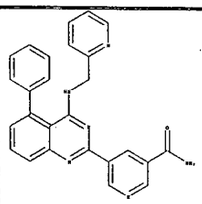
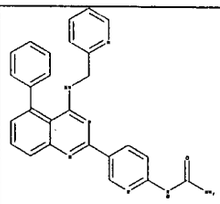
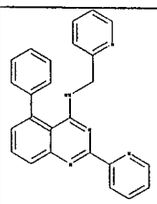
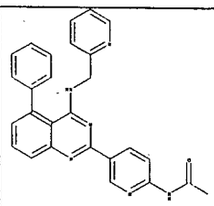
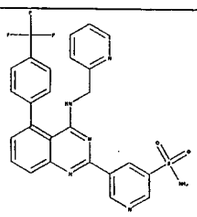
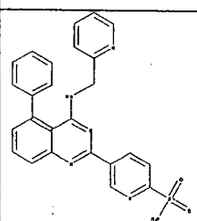


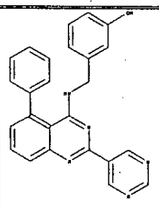
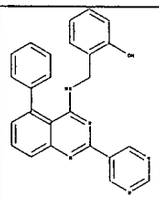
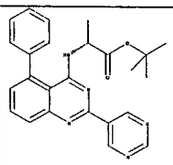
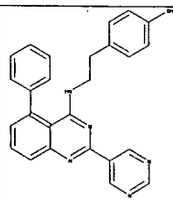
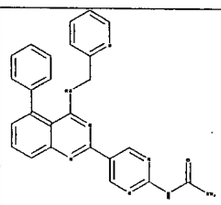
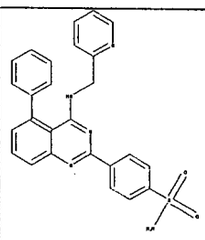
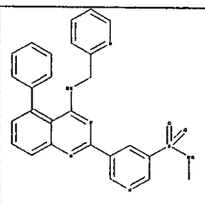
[00297] A solution of the ethyl 5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)isoxazole-3-carboxylate (from example 209, 0.075 g, 0.17 mmol) in NH_3 (2.0 M in MeOH, 5 mL) was heated at 60°C in a sealed vessel for 16 h. After this time, the reaction mixture was allowed to cool to room temperature. Once at the prescribed temperature, the solid formed was filtered and washed with ice cooled methanol to provide Example 224 (31 mg, 44 % yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.29 (s, 1H), 8.21 (d, 1H, J = 2Hz), 7.87-7.95 (m, 3H), 7.73 (dt, 1H, J = 1.6, 8Hz), 7.45-7.64 (m, 5H), 7.37 (dt, 2H, J = 1.6, 6.8Hz, 2H), 7.25 (dd, 1H, J = 6.0, 7.2Hz), 4.70 (d, 2H, J = 4Hz). LCMS Method W: retention time 1.817 min; [M+1] = 423.2; HPLC Method A1: purity 99.3 %, retention time = 7.31 min.

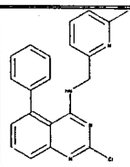
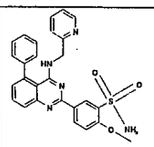
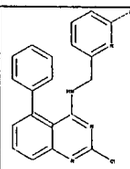
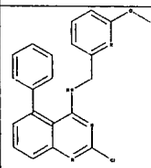
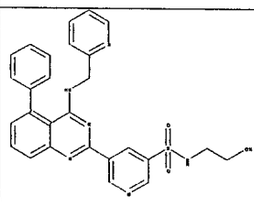
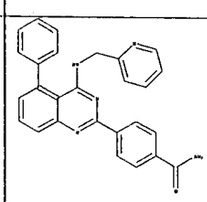
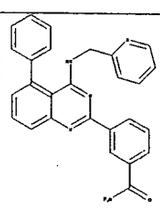
EXAMPLES 225 TO 322

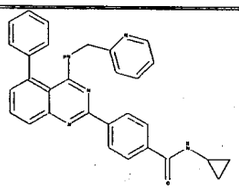
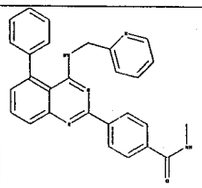
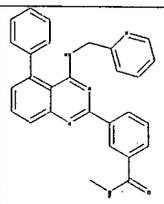
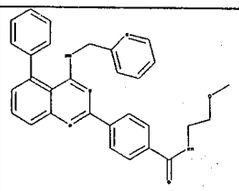
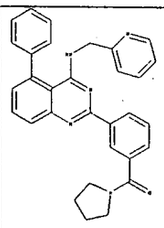
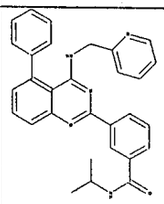
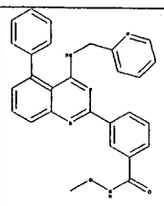
[00298] Examples 225 to 322 were synthesized via similar procedures described above. HPLC/MS data for each compound was collected using methods E-Z1 and the molecular mass determined by MS (ES) by the formula m/z. Both the retention time and MS data for Examples 225 to 322 are listed in Table 1c, wherein MW = molecular weight.

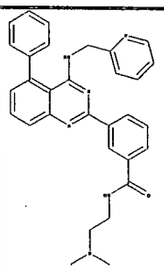
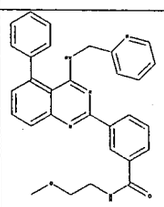
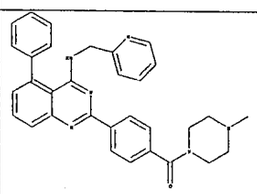
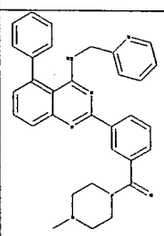
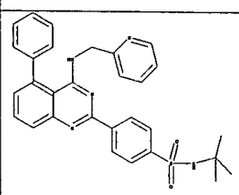
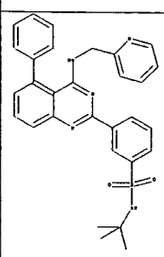
TABLE 1c

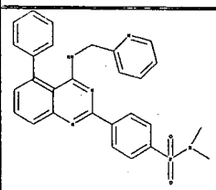
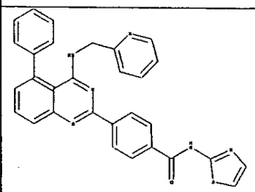
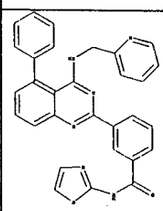
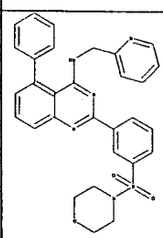
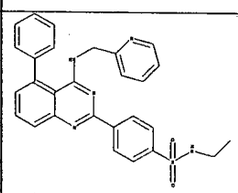
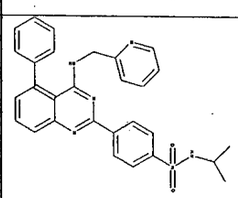
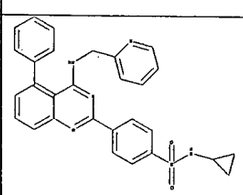
Example	Structure	MW	LCMS Data	LCMS Method
225		432.477	[M+1] 433.0 Rt1.86 min	E
226		447.491	[M+1] 448.0 Rt1.50 min	O
227		389.452	[M+1] 390.0 Rt1.58 min	O
228		446.503	[M+1] 447.0 Rt1.49 min	O
229		536.528	[M+1] 537.0 Rt1.73 min	O
230		468.53	[M+1] 469.0 Rt1.41 min	O

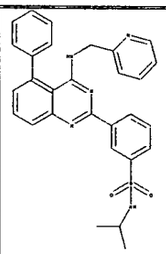
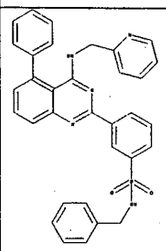
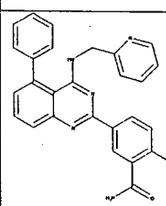
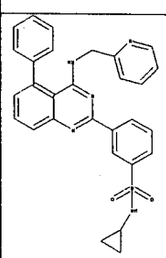
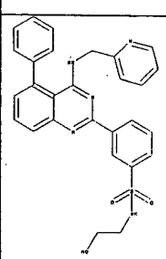
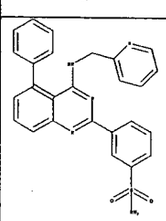
Example	Structure	MW	LCMS Data	LCMS Method
231		405.451	[M+1] 406.2 Rt2.50 min	Z1
232		405.451	[M+1] 406.2 Rt2.58 min	Z1
233		427.498	[M+1] 428.2 Rt3.12 min	Z1
234		419.478	[M+1] 420.2 Rt2.56 min	Z1
235		448.479	[M+1] 449.2 Rt1.89 min	Y
236		467.542	[M+1] 468.2 Rt1.98 min	Y
237		482.557	[M+1] 483.2 Rt1.99 min	Y

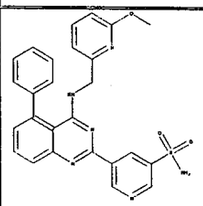
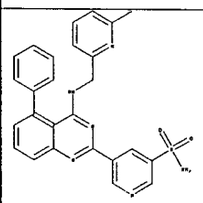
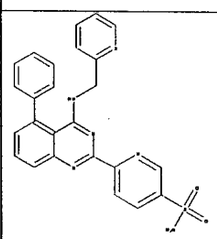
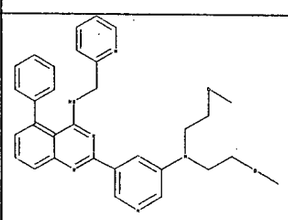
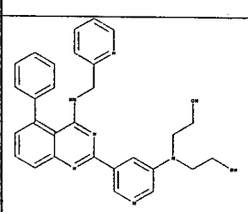
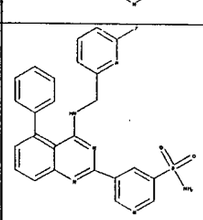
Example	Structure	MW	LCMS Data	LCMS Method
238		360.839	[M+1] 361.20 Rt1.55 min	T
239		497.568	[M+1] 498.2 Rt1.48 min	T
240		364.803	[M+1] 365.2 Rt2.05 min	T
241		376.839	[M+1] 377.2 Rt2.14 min	T
242		512.583	[M+1] 513.2 Rt1.80 min	Y
243		431.489	[M+1] 432.2 Rt2.40 min	Z1
244		431.489	[M+1] 432.2 Rt2.40 min	Z1

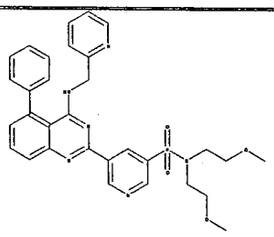
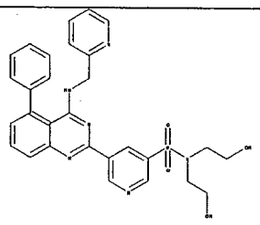
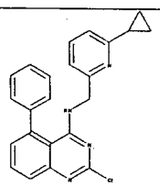
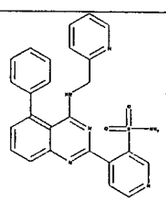
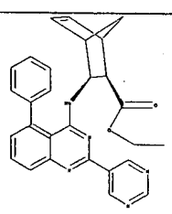
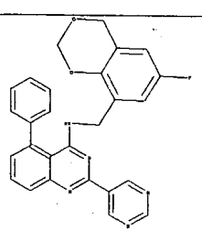
Example	Structure	MW	LCMS Data	LCMS Method
245		471.552	[M+1] 472.2 Rt2.68 min	Z1
246		445.515	[M+1] 446.2 Rt2.50 min	Z1
247		445.515	[M+1] 446.2 Rt2.53 min	Z1
248		489.568	[M+1] 490.2 Rt2.59 min	Z1
249		485.579	[M+1] 486.2 Rt2.84 min	Z1
250		473.568	[M+1] 474.2 Rt2.87 min	Z1
251		461.515	[M+1] 462.2 Rt2.52 min	Z1

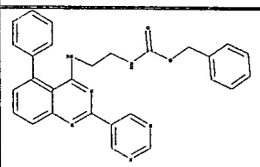
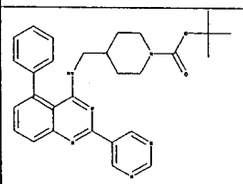
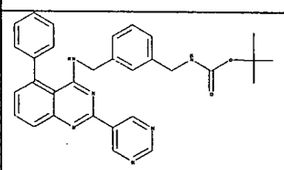
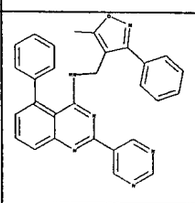
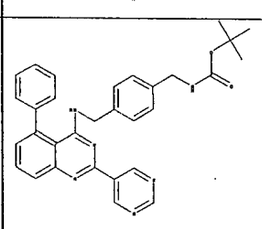
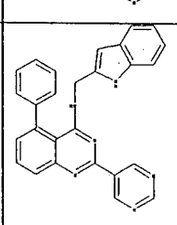
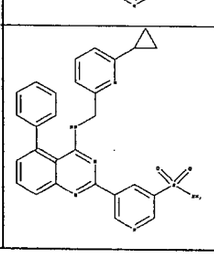
Example	Structure	MW	LCMS Data	LCMS Method
252		502.609	[M+1] 503.2 Rt2.57 min	Z1
253		489.568	[M+1] 490.2 Rt2.63 min	Z1
254		514.62	[M+1] 515.2 Rt2.58 min	Z1
255		514.62	[M+1] 515.2 Rt2.58 min	Z1
256		523.649	[M+1] 524.2 Rt3.24 min	Z1
257		523.649	[M+1] 524.2 Rt3.23 min	Z1

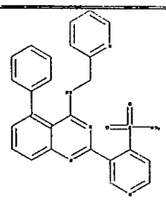
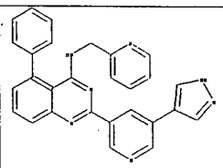
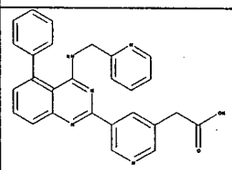
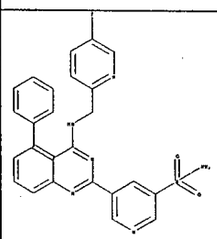
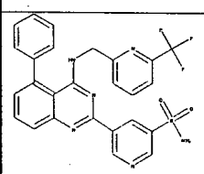
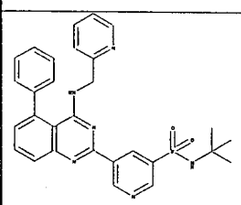
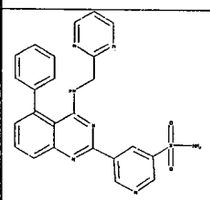
Example	Structure	MW	LCMS Data	LCMS Method
258		495.595	[M+1] 496.2 Rt3.13 min	Z1
259		514.6	[M+1] 515.2 Rt2.99 min	Z1
260		514.6	[M+1] 515.2 Rt3.04 min	Z1
261		537.632	[M+1] 538.2 Rt3.05 min	Z1
262		495.595	[M+1] 496.2 Rt2.96 min	Z1
263		509.622	[M+1] 510.2 Rt3.10 min	Z1
264		507.606	[M+1] 508.2 Rt3.01 min	Z1

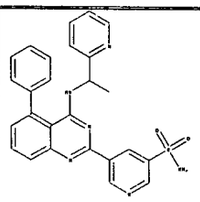
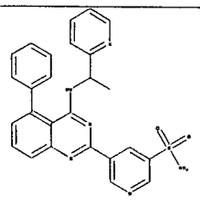
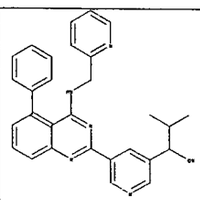
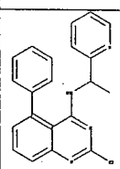
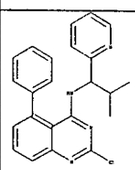
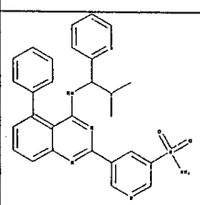
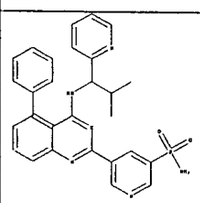
Example	Structure	MW	LCMS Data	LCMS Method
265		509.622	[M+1] 510.2 Rt3.09 min	Z1
266		557.665	[M+1] 558.2 Rt3.23 min	Z1
267		449.479	[M+1] 450.2 Rt2.54 min	Z1
268		507.606	[M+1] 508.2 Rt2.99 min	Z1
269		511.595	[M+1] 512.2 Rt2.50 min	Z1
270		467.542	[M+1] 468.2 Rt2.53 min	Z1

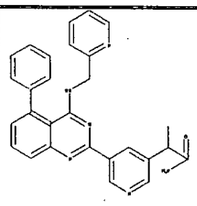
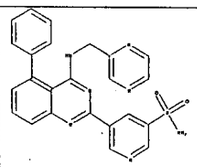
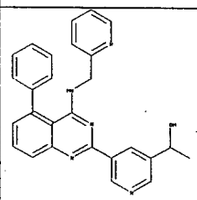
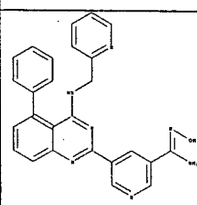
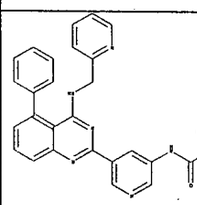
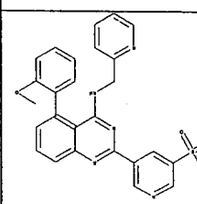
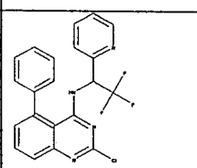
Example	Structure	MW	LCMS Data	LCMS Method
271		498.556	[M+1] 499.2 Rt2.03 min	W
272		482.557	[M+1] 483.2 Rt1.91 min	W
273		468.53	[M+1] 469.2 Rt1.52 min	T
274		520.625	[M+1] 521.2 Rt1.76 min	T
275		492.572	[M+1] 493.4 Rt1.73 min	Y
276		486.521	[M+1] 487.2 Rt1.95 min	W

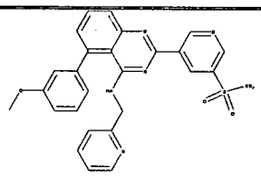
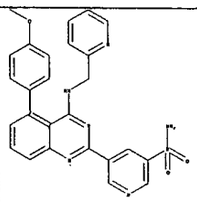
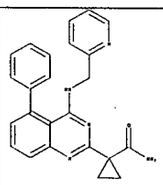
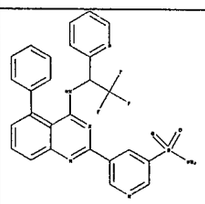
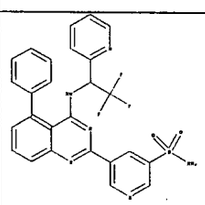
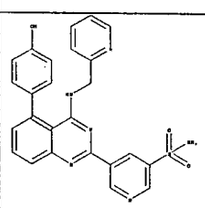
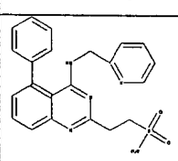
Example	Structure	MW	LCMS Data	LCMS Method
277		584.689	[M+1] 585.2 Rt1.83 min	T
278		556.635	[M+1] 557.2 Rt1.56 min	T
279		386.877	[M+1] 387.2 Rt2.17 min	Y
280		468.53	[M+1] 469.2 Rt1.84 min	Y
281		463.53	[M+1] 464.2 Rt3.16 min	Z1
282		465.478	[M+1] 466.2 Rt3.00 min	Z1

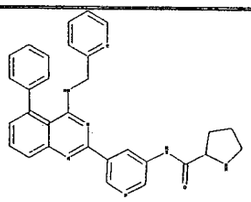
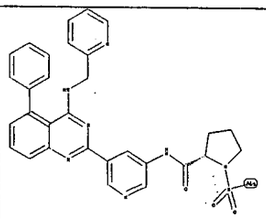
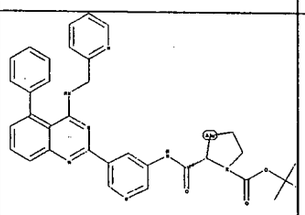
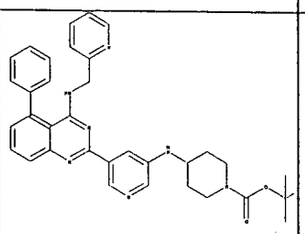
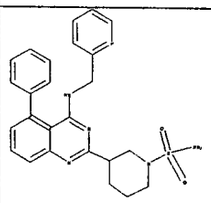
Example	Structure	MW	LCMS Data	LCMS Method
283		476.529	[M+1] 477.2 Rt2.74 min	Z1
284		496.603	[M+1] 497.2 Rt3.34 min	Z1
285		518.609	[M+1] 519.2 Rt3.17 min	Z1
286		470.525	[M+1] 471.2 Rt2.97 min	Z1
287		518.609	[M+1] 519.2 Rt3.16 min	Z1
288		428.488	[M+1] 429.2 Rt3.01 min	Z1
289		508.594	[M+1] 509.2 Rt1.58 min	T

Example	Structure	MW	LCMS Data	LCMS Method
290		468.53	[M+1] 469.2 Rt1.42 min	T
291		455.513	[M+1] 456.2 Rt1.86 min	Y
292		447.488	[M+1] 448.2 Rt1.36 min	W
293		486.521	[M-1] 485.0 Rt1.93 min	Y
294		536.528	[M+1] 537.0 Rt1.96 min	T
295		524.637	[M-1] 523.2 Rt2.10 min	Y
296		469.518	[M+1] 470.2 Rt1.64 min	T

Example	Structure	MW	LCMS Data	LCMS Method
297		482.557	[M+1] 483.2 Rt1.66 min	T
298		482.557	[M+1] 483.2 Rt1.65 min	T
299		461.558	[M+1] 462.2 Rt1.78 min	T
300		360.839	[M+1] 361.0 Rt1.87 min	T
301		388.893	[M+1] 389.2 Rt1.98 min	T
302		510.61	[M+1] 511.2 Rt1.79 min	T
303		510.61	[M+1] 511.2 Rt1.79 min	T

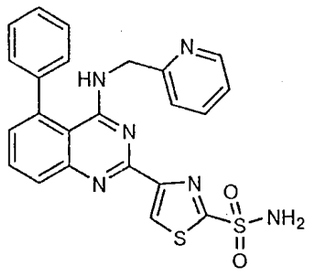
Example	Structure	MW	LCMS Data	LCMS Method
304		460.53	[M+1] 461.0 Rt1.78 min	Y
305		469.518	[M+1] 470.0 Rt1.72 min	W
306		433.504	[M+1] 434.2 Rt1.60 min	V
307		447.491	[M+1] 447.9 Rt1.79 min	Y
308		500.475	[M-1] 499.0 Rt1.75 min	V
309		498.556	[M+1] 499.2 Rt1.83 min	W
310		414.811	[M+1] 415.0 Rt2.16 min	T

Example	Structure	MW	LCMS Data	LCMS Method
311		498.556	[M+1] 499.2 Rt1.87 min	W
312		498.556	[M+1] 499.2 Rt1.64 min	V
313		395.456	[M+1] 396.2 Rt1.43 min	T
314		536.528	[M+1] 537.2 Rt2.05 min	T
315		536.528	[M+1] 537.2 Rt2.05 min	T
316		484.53	[M+1] 485.2 Rt1.69 min	Y
317		419.499	[M-1] 418.0 Rt1.73 min	Y

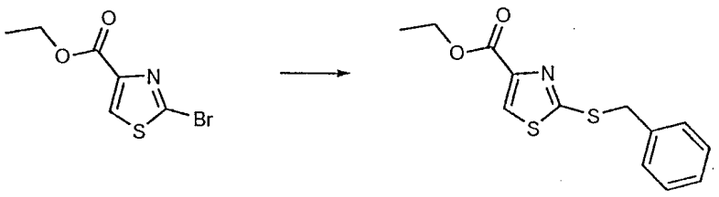
Example	Structure	MW	LCMS Data	LCMS Method
318		501.582	[M+1] 502.2 Rt1.58 min	V
319		579.672	[M+1] 580.2 Rt1.87 min	W
320		601.697	[M-1] 600.2 Rt2.16 min	W
321		587.714	[M+1] 588.2 Rt1.865 min	V
322		474.578	[M+1] 475.2 Rt1.84 min	W

EXAMPLE 323

4-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)thiazole-2-sulfonamide

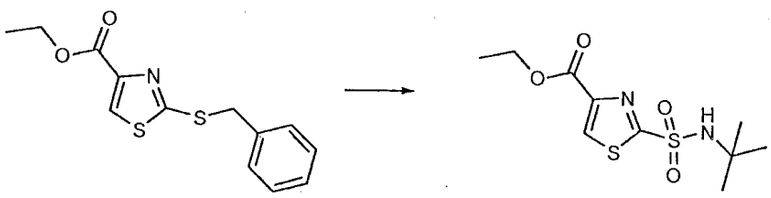


Step 1. Preparation of ethyl 2-(benzylthio)thiazole-4-carboxylate



[00299] To a solution of ethyl 2-bromothiazole-4-carboxylate (2.0g, 8.40mmol) in DMF (15 mL) was added K_2CO_3 (1.16 g, 8.40 mmol) followed by benzyl mercaptan (1.07 g, 8.40 mmol) in DMF (5 mL) over 20min. Upon completion of addition, the reaction mixture was stirred at RT for 16 h. After this time, the reaction mixture was diluted with water and extracted in EtOAc. The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting concentrate was purified by silica gel chromatography (10 % EtOAc in hexane) to provide ethyl 2-(benzylthio)thiazole-4-carboxylate (2.0 g, 87 % yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.42 (s, 1H); 7.47-45 (m, 2H); 7.36-7.28 (m, 3H); 4.52 (s, 2H); 4.31(q, 2H, J = 7.2Hz); 1.31 (t, 3H, J = 7.2Hz).

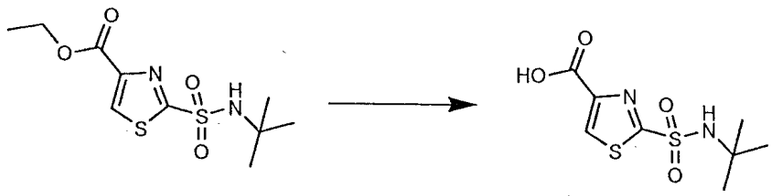
Step 2. Preparation of ethyl 2-(N-tert-butylsulfamoyl)thiazole-4-carboxylate



[00300] A solution of ethyl 2-(benzylthio)thiazole-4-carboxylate (2.0 g, 7.10 mmol) in CCl_4/H_2O (100/10 mL) was cooled to 0-5 ^{0}C. Chlorine gas was bubbled

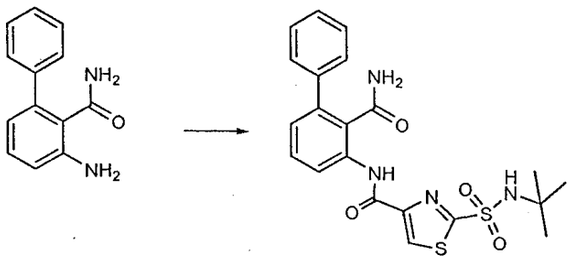
through the solution for 30 min. After this time, the excess chlorine gas was evaporated by flushing with a stream of nitrogen. The reaction mixture was then diluted with dichloromethane and washed with brine. The combined organic layers were dried over Na_2SO_4, filtered and concentrated to yield the crude sulfonyl chloride. The crude sulfonyl chloride was dissolved in THF (50mL) followed by the addition of tert-butyl amine (10 mL) in sealed tube. The contents of the tube were heated to 60^0C for 16h. At the conclusion of this period, the volatiles were evaporated. The resulting residue was washed with water and extracted into EtOAc. The combined organic layers were dried over Na_2SO_4, filtered and concentrated to provide ethyl 2-(N-tert-butylsulfamoyl)thiazole-4-carboxylate (1.8g, 90% yield) as off white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.78 (s, 1H); 8.0 (br s, 1H); 4.34 (q, 2H, J = 7.2Hz); 1.31 (t, 3H, J = 7.2Hz); 1.18 (s, 9H).

Step 3. Preparation of ethyl 2-(N-tert-butylsulfamoyl)thiazole-4-carboxylate



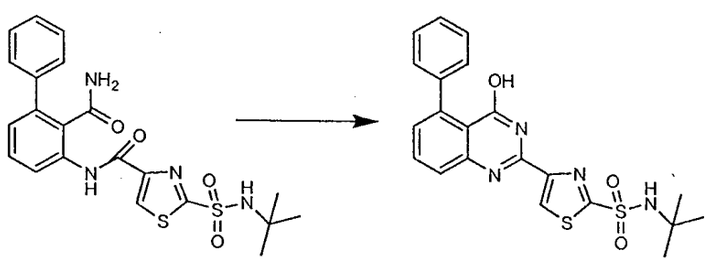
[00301] To a solution of ethyl 2-(N-tert-butylsulfamoyl)thiazole-4-carboxylate (1.8g, 6.1 mmol) in 50mL THF-EtOH (1:1) was added LiOH (.07g, 18.3mmol). The resulting mixture was stirred for 4h. After this time, the reaction mixture was neutralized with HCl (1.0 M, aq), diluted with water and then extracted into EtOAc. The combined organic layers were dried over Na_2SO_4, filtered and concentrated to provide ethyl 2-(N-tert-butylsulfamoyl)thiazole-4-carboxylate (1.6g, 99% yield) as a white solid. LCMS Method V: retention time 0.93 min; [M+1] = 263.0.

Step 4. Preparation of 2-(N-tert-butylsulfamoyl)-N-(2-carbamoylbiphenyl-3-yl)thiazole-4-carboxamide



[00302] To a solution of 2-(N-tert-butylsulfamoyl)thiazole-4-carboxylic acid (0.56 g, 2.1 mmol) in DCM (50 mL) was added HATU (1.41 g, 2.8 mmol) and DIPEA (1.04 ml, 5.6 mmol). The reaction mixture was stirred at room temperature for 1h and then 3-aminobiphenyl-2-carboxamide (from example 218, 0.3 g, 1.4 mmol) was added. The resulting solution was stirred for an additional 16h. After this time, the reaction mixture was washed with water, dried, filtered and concentrated under reduced pressure to yield a residue. The residue was purified by silica gel chromatography (30% EtOAc in hexane) to provide 2-(N-tert-butylsulfamoyl)-N-(2-carbamoylbiphenyl-3-yl)thiazole-4-carboxamide (0.11g, 17% yield) as white solid. LCMS Method V: retention time 1.85 min; [M+1] = 459.2.

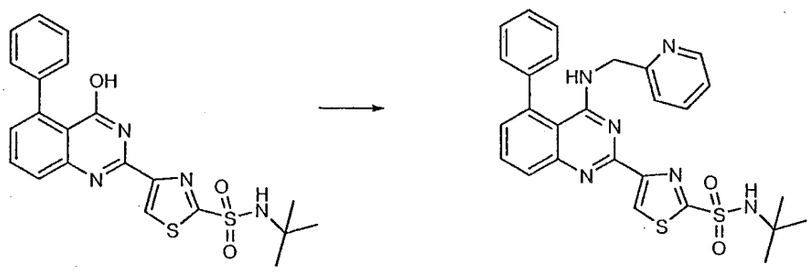
Step 5. Preparation of (N-tert-butyl-4-(4-hydroxy-5-phenylquinazolin-2-yl)thiazole-2-sulfonamide



[00303] To a solution 2-(N-tert-butylsulfamoyl)-N-(2-carbamoylbiphenyl-3-yl)thiazole-4-carboxamide (0.11 g, 0.24 mmol) in methanol (10 mL) was added NaOMe (0.25 ml, 25 % in MeOH, 1.2 mmol). The resulting mixture was stirred at RT for 16h. After this time, the reaction mixture was concentrated, diluted with ethyl acetate and washed with water. The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified

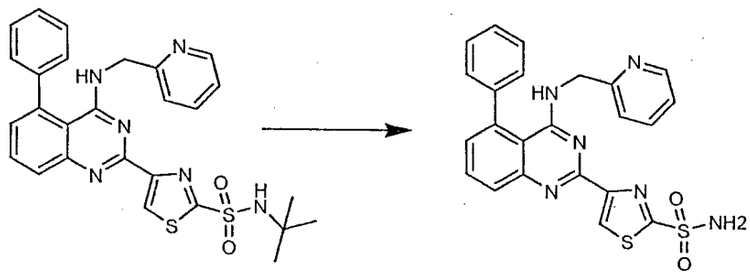
by silica gel chromatography (40 % EtOAc in hexane) to provide (N-tert-butyl-4-(4-hydroxy-5-phenylquinazolin-2-yl)thiazole-2-sulfonamide (0.10 g, 100 % yield) as a white solid. LCMS Method V: retention time 2.01 min; [M+1] = 441.2.

Step 6. Preparation of 5-phenyl-N-(pyridin-2-ylmethyl)-2-(2,2,5-trimethyl-1,3-dioxan-5-yl)quinazolin-4-amine



[00304] To a solution of 5-phenyl-2-(2,2,5-trimethyl-1,3-dioxan-5-yl)quinazolin-4(3H)-one (0.22 g, 0.62 mmol) in MeCN (10 mL) at room temperature was added DBU (0.24 g, 1.57 mmol) and BOP reagent (0.36 g, 0.81 mmol). Upon completion of addition, the reaction mixture was stirred for 30min. Aminomethylpyridine (0.11 ml, 1.13 mmol) was added and the resulting mixture was stirred for an additional 16h. After this time, the reaction mixture was concentrated and purified by silica gel column chromatography (2 % MeOH in DCM) to provide 5-phenyl-N-(pyridin-2-ylmethyl)-2-(2,2,5-trimethyl-1,3-dioxan-5-yl)quinazolin-4-amine (0.18 g, 68 % yield) as a white solid. LCMS Method V: retention time 2.21 min, [M+1] = 531.2.

Step 7. Example 323

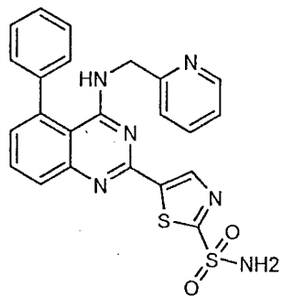


[00305] A solution of N-tert-butyl-4-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)thiazole-2-sulfonamide (0.05 g 0.10 mmol) in TFA

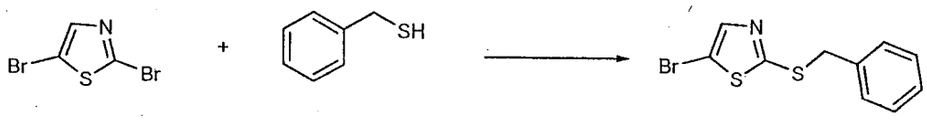
(10 mL) was heated at 50 °C for 8h. After this time, the TFA was evaporated off under reduced pressure to yield a residue. The residue was made basic by the addition of 10% sodium bicarbonate solution and then extracted into DCM. The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by recrystallization using DCM/hexane to provide Example 323 (30 mg, 78 % yield) as a brownish yellow solid. ^{1}H NMR (400 MHz, DMSO-d6, δ): 8.80 (s, 1H); 8.25 (s, 1H); 8.19 (br s, 1H); 7.90-7.80 (m, 2h); 7.65 (dt, 1H, J = 1.6, 6.8Hz); 7.60-7.48 (m, 5H); 7.32-7.20 (m, 3H); 6.78 (t, 1H, J = 4Hz); 4.71 (d, 2H, J = 4Hz). LCMS Method R: retention time 1.65 min, [M+1] = 472.8; HPLC Method A1: purity 95.8 %, retention time = 12.5 min.

EXAMPLE 324

5-(5-Phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)thiazole-2-sulfonamide



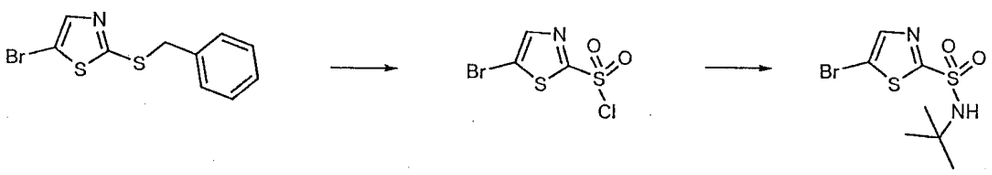
Step 1. Preparation of 2-(benzylthio)-5-bromothiazole



[00306] To a solution of 2,5-dibromothiazole (2.0 g, 8.23 mmol) in DMF (15 mL) was added K_2CO_3 (1.16 g, 8.40 mmol) followed by benzyl mercaptan (1.07 g, 8.40 mmol) in DMF (10 mL) over a period of 20 min. The reaction mixture was stirred at RT for over night. After this time, the reaction mixture was diluted with water and extracted in EtOAc. The combined organic layers were dried over Na_2SO_4, filtered

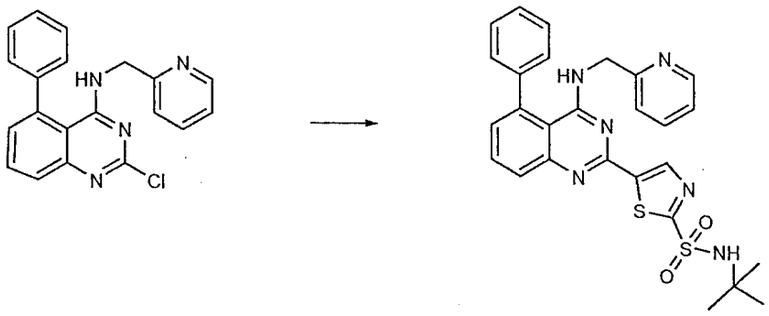
and concentrated under reduced pressure. The resulting crude product was purified by silica gel chromatography (0.2 % EtOAc in hexane) to yield 2-(benzylthio)-5-bromothiazole (2.3 g, 97.5 % yield) as a brown solid. ^{1}H NMR (400 MHz, DMSO-d6, δ): 7.56 (s, 1H); 7.25-7.36 (m, 5H); 4.39 (s, 2H). ^{1}H LCMS Method V: Retention time 2.319 min, [M+1] = 286.

Step 2. Preparation of 5-bromo-N-tert-butylthiazole-2-sulfonamide



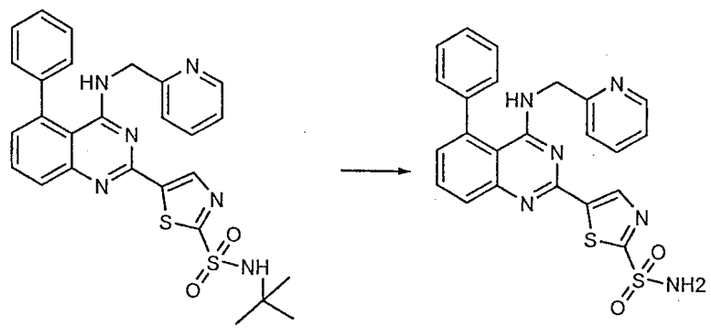
[00307] A solution of 2-(benzylthio)-5-bromothiazole (2.3g 8.00 mmol) was dissolved in CCl_4 / H_2O (100/10 mL) and then cooled to 0-5 °C. Chlorine gas was bubbled through the reaction mixture for 30 min. After this time, the excess chlorine gas was evaporated by flushing the reaction mixture with a stream of nitrogen. The reaction mixture was diluted with dichloromethane and washed with brine. The combined organic layers were dried over Na_2SO_4, filtered and concentrated to provide the crude sulfonyl chloride. The crude sulfonyl chloride was dissolved in THF (50mL) and then tert-butyl amine (10 mL) was added in sealed tube. The contents of the tube were heated to 60 °C for 16 h. After this time, the volatiles were evaporated and washed with water and extracted into EtOAc. The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The resulting residue was purified by silica gel chromatography (10 % EtOAc/hexane) to provide 5-bromo-N-tert-butylthiazole-2-sulfonamide (1.0 g, 41.5 %yield) as a white solid. NMR (400 MHz, DMSO-d6, δ): 8.41 (s, 1H); 8.17 (s, 1H); 1.25 (s, 9H). LCMS Method V: Retention time 1.861min, [M-1] = 297.

Step 3... Preparation of N-tert-butyl-5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)thiazole-2-sulfonamide



[00308] To a stirring suspension of 5-bromo-N-tert-butylthiazole-2-sulfonamide (0.50 g, 1.67 mmol) in 1,4-dioxane (10 mL) was added lithium chloride (0.210 g, 5.03 mmol), followed by hexamethylditin (0.820 g, 2.50 mmol). After degassing with nitrogen, $Pd(TPP)_4$ (0.19 g, 0.16 mmol) was added. The resultant suspension was stirred for over night at RT. 2-Chloro-5-phenyl-N-(pyridin-2-ylmethyl)quinazolin-4-amine(0.46 g, 1.33 mmol) was dissolved in 1,4-dioxane(3 mL) and then added to the reaction mixture. Upon completion of addition, the reaction mixture was heated at 90 ^{0}C for 24h. After this time, the solvent was evaporated, water was added and the mixture was extracted with DCM. The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The resulting residue was purified by recrystallization with ethyl acetate and further purified by preparative HPLC (method H) to provide N-tert-butyl-5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)thiazole-2-sulfonamide (32 mg, 4.2 %) as a yellow solid. LCMS Method V: Rt 2.47 min; [M+1] = 531.2; HPLC Method A1: purity 97.3%, retention time = 10.89min.

Step 4. Example 324



[00309] A solution of N-tert-butyl-5-(5-phenyl-4-(pyridin-2-ylmethylamino)quinazolin-2-yl)thiazole-2-sulfonamide (0.03 g 0.05 mmol) in TFA (5 ml) was heated at 80 °C for 8 h. After this time, the TFA was evaporated. The reaction mixture was basified with 10 % sodium bicarbonate solution and then extracted in DCM. The combined organic layers were dried over Na_2SO_4, filtered and concentrated to yield a residue. The residue was purified by recrystallization with DCM/hexane to provide Example 324 (23 mg, 86 % yield) as a brownish yellow solid. ^{1}H NMR (400 MHz, DMSO-d6, δ): 8.68 (s, 1H); 8.21 (s, 1H); 8.19 (br s, 1H); 7.83-7.80 (m, 2h); 7.62 (dt, 1H, J = 1.6, 6.8Hz); 7.61-7.49 (m, 5H); 7.32-7.28 (m, 2H); 7.23-7.20 (m, 1H); 6.94 (t, 1H, J = 4Hz); 4.68 (d, 2H, J = 4Hz). LCMS Method T: Rt 1.63 min; [M+1] = 475.0; HPLC Method A1: purity 99.0 %, retention time = 8.05 min.

[00310] It is noted that the proceeding examples, while illustrative of the present invention, are not in sequential order and some example numbers may be missing.

UTILITY

[00311] In general, compounds of the present invention, such as particular compounds disclosed in the preceding examples, have been shown to inhibit the K_v1 subfamily of voltage-gated K+ channels (for example, by displaying % inhibition values $\geq$ 29%, preferably $\geq$ 30%, more preferably $\geq$ 40%, even more preferably $\geq$ 50%, at 0.3 micromolar concentration in an assay such as those set forth below). By displaying activity as inhibitors of the K_v1 subfamily of voltage-gated K+ channels, compounds of the present invention are expected to be useful in the treatment of human diseases associated with the K_v1 subfamily of voltage-gated K+ channels.

[00312] Assays to determine the degree of activity of a compound as an I_{Kur} inhibitor are well known in the art and are described in references such as *J. Gen. Physiol.*, 101(4):513-543 (Apr. 1993), and *Br. J. Pharmacol.*, 115(2):267-274 (May 1995).

[00313] Assays to determine the degree of activity of a compound as an inhibitor of other members of the K_v1 subfamily are also well known in the art. For example, inhibition of $K_v1.1$, $K_v1.2$ and $K_v1.3$ can be measured using procedures described by

Grissmer, S. et al., *Mol. Pharmacol.*, 45(6):1227-1234 (Jun. 1994); inhibition of $K_v1.4$ can be measured using procedures described by Petersen, K.R. et al., *Pflugers Arch.*, 437(3):381-392 (Feb. 1999); inhibition of $K_v1.6$ can be measured using procedures described by Bowlby, M.R. et al., *J. Neurophysiol.* 73(6):2221-2229 (Jun. 1995); and inhibition of $K_v1.7$ can be measured using procedures described by Kalman, K. et al., *J. Biol. Chem.*, 273(10):5851-5857 (Mar. 6, 1998).

[00314] Compounds of the present invention were tested in one of the assays described immediately above and the results shown in Table 2 below were obtained.

Table 2

Example	Kv 1.5 (% inhibition at 0.3 uM)
7	95.7
22	60.4
29	65.3
31	98.2
32	53.1
38	61.3
40	59.8
42	96.4
46	98.7
50	96.1
97	98.7
105	98.7
107	50.3
108	98.1
110	51.8
111	61.5
130	96.2
134	98.4
137	55.6

[00315] Find below in Table 3 data for disclosed compounds (See U.S. Patent No. 7,713,983). It is believed that this data demonstrates the unexpected ability of the compounds of the present invention to significantly increase the inhibition of the K_v1 subfamily of voltage-gated K+ channels.

TABLE 3

Compound	Kv 1.5 (% inhibition at 0.3 uM)	Replicates
Example 578 U.S. 7,713,983	20.5 ± 2.3	2
Example 580 U.S. 7,713,983	5.3 ± 5.1	2
Example 68 U.S. 7,713,983	8.5 ± 6.9	2
Example 82 U.S. 7,713,983	5.6 ± 3.8	2

[00316] In addition, compounds of the present invention, such as particular compounds disclosed in the preceding examples, were evaluated for their effectiveness as inhibitors of kinase receptor activity. The compounds were tested in the assay(s) set forth below for inhibition of kinase activity and results are shown in Table 4. Based on the results, it is believed that the compounds of the present invention, such as particular compounds disclosed in the preceding examples, are not effective in inhibiting kinase receptor activity and therefore would not be effective as inhibitors or modulators of kinase receptor activity.

Caliper Kinase Assay

[00317] The analyses were performed in U-bottom 384-well plates. The final assay volume was 30 µl prepared from 15 µl additions of enzyme and substrates (fluoresceinated peptide and ATP) and test compounds in assay buffer (20 mM HEPES pH 7.4, 10 mM $MgCl_2$, 0.015% Brij35 and 4 mM DTT). The reaction was

initiated by the combination of purified protein kinase with substrates and test compounds. The reaction was incubated at room temperature for 60 min. and terminated by adding 30 µl of 35 mM EDTA to each sample. The reaction mixture was analyzed on the Caliper LABCHIP® 3000 (Caliper, Hopkinton, MA) by electrophoretic separation of the fluorescent substrate and phosphorylated product. Inhibition data were calculated by comparison to no enzyme control reactions for 100% inhibition and vehicle-only reactions for 0% inhibition. The ATP was used at a final concentration equivalent to the Km and the peptide substrate concentration was 1.5 µM. Dose response curves were generated to determine the concentration required to inhibit 50% of kinase activity (IC_{50}). Compounds were dissolved at 10 mM in dimethylsulfoxide (DMSO) and evaluated at eleven concentrations. IC_{50} values were derived by non-linear regression analysis.

TABLE 4

Example	LLE Flt3 (IC50, uM)	LLE GSK3B (IC50, uM)	LLE IGF1R (IC50, uM)	LLE IKKE (IC50, uM)	LLE IRAK-4 (IC50, uM)	LLE IRAK1 (IC50, uM)	LLE mAurA (IC50, uM)	LLE PIM1 (IC50, uM)	LLE_ABL1 (%INH, 50uM)	LLE_AURORA-B (IC50, uM)
1	—	50.00	—	50.00	50.00	50.00	—	—	—	50.00
7	—	50.00	—	—	50.00	—	—	—	—	—
19	10.11	5.15	17.58	50.00	18.69	—	39.84	33.81	32.37	—

Example	LLE_BMX (IC50, uM)	LLE_BTK (IC50, uM)	LLE_CDK2E (IC50, uM)	LLE_CDK5 (IC50, uM)	LLE_CDK5/p25 (IC50, uM)	LLE_CK1A1(IC50, uM)	LLE_CK2A1(IC50, uM)	LLE_CK2A2 (IC50, uM)	LLE_IGF1R (IC50, uM)	LLE_IRAK1 (IC50, uM)
1	50.00	50.00	50.00	—	—	—	—	—	—	50.00
7	50.00	50.00	50.00	—	—	—	—	50.00	—	—
19	—	19.17	50.00	50.00	50.00	50.00	50.00	25.52	17.58	—

000405

Example	LLE_ITK (IC50, uM)	LLE_JAK 1 (IC50, uM)	LLE_JAK 2 (IC50, uM)	LLE_JAK 3 (IC50, uM)	LLE_Lck (IC50, uM)	LLE_LYNA (IC50, uM)	LLE_mAur A (IC50, uM)	LLE_PIM1 (IC50, uM)	LLE_PLK 1 (IC50, uM)	LLE_SRC (IC50, nM)
1	50.00	—	23.87	50.00	50.00	50.00	—	—	—	—
7	50.00	—	50.00	50.00	50.00	50.00	—	—	—	—
19	—	50.00	17.79	23.84	—	—	39.84	33.81	50.00	50.00

Example	LLE_TAK1 (IC50, uM)	LLE_TBK1 (IC50, uM)	LLE_TEC (IC50, uM)	LLE_TPL2 CAL (IC50, uM)	LLE_TXK (IC50, uM)	LLE_TYK2_887 (IC50, uM)
1	50.00	50.00	50.00	—	50.00	50.00
7	—	—	50.00	—	—	50.00
19	—	—	—	11.90	—	50.00

[00318] In view of the foregoing, it is believed that compounds of the present invention show unexpected advantages over compounds previously disclosed in the art. It is believed that compounds of the present invention demonstrate a desirable combination of K_v1 subfamily inhibitory activity and minimal potency against kinases or Na+ ion channel. In addition, it is believed that Example 7 demonstrates a desirable combination of K_v1 subfamily inhibitory activity and pharmacological characteristics including a surprisingly low degree of brain penetration across species in combination with indications of high efficacy and improved safety criteria, for example, improved ion channel selectivity as measured by hERG and Na+ ion channel studies.

[00319] Compounds within the scope of the present invention inhibit the K_v1 subfamily of voltage-gated K+ channels, and as such are believed to be useful in the treatment and/or prevention of various disorders: cardiac arrhythmias, including supraventricular arrhythmias, atrial arrhythmias, atrial flutter, atrial fibrillation, complications of cardiac ischemia, and use as heart rate control agents; angina pectoris including relief of Prinzmetal's symptoms, vasospastic symptoms and variant symptoms; gastrointestinal disorders including reflux esauphagitis, functional dispepsia, motility disorders (including constipation and diarrhea), and irritable bowel syndrome; disorders of vascular and visceral smooth muscle including asthma, chronic obstructive pulmonary disease, adult respiratory distress syndrome, peripheral vascular disease (including intermittent claudication), venous insufficiency, impotence, cerebral and coronary spasm and Raynaud's disease; inflammatory and immunological disease including inflammatory bowel disease, rheumatoid arthritis, graft rejection, asthma. chronic obstructive pulmonary disease, cystic fibrosis and atherosclerosis; cell proliferative disorders including restenosis and cancer (including leukemia); disorders of the auditory system; disorders of the visual system including macular degeneration and cataracts; diabetes including diabetic retinopathy, diabetic nephropathy and diabetic neuropathy; muscle disease including myotonia and wasting; peripheral neuropathy; cognitive disorders; migraine; memory loss including Alzheimer's and dementia; CNS mediated motor dysfunction including Parkinson's disease, and ataxia; epilepsy; and other ion channel mediated disorders.

[00320] As inhibitors of the K_v1 subfamily of voltage-gated K+ channels compounds of the present invention are believed to be useful to treat a variety of further disorders including resistance by transplantation of organs or tissue, graft-versus-host diseases brought about by medulla ossium transplantation, rheumatoid arthritis, systemic lupus erythematosus, Hashimoto's thyroiditis, multiple sclerosis, myasthenia gravis, type I diabetes uveitis, juvenile-onset or recent-onset diabetes mellitus, posterior uveitis, allergic encephalomyelitis, glomerulonephritis, infectious diseases caused by pathogenicmicroorganisms, inflammatory and hyperproliferative skin diseases, psoriasis, atopical dermatitis, contact dermatitis, eczematous dermatitises, seborrhoeis dermatitis, Lichen planus, Pemphigus, bullous pemphigoid, Epidermolysis bullosa, urticaria, angioedemas, vasculitides, erythemas, cutaneous eosinophilias, Lupus erythematosus, acne, Alopecia areata, keratoconjunctivitis, vernal conjunctivitis, uveitis associated with Behcet's disease, keratitis, herpetic keratitis, conical cornea, dystrophia epithelialis corneae, corneal leukoma, ocular pemphigus, Mooren's ulcer Scleritis, Graves' opthalmopathy, Vogt-Koyanagi-Harada syndrome, sarcoidosis, pollen allergies, reversible obstructive airway disease, bronchial asthma, allergic asthma, intrinsic asthma, extrinsic asthma, dust asthma, chronic or inveterate asthma, late asthma and airway hyper-responsiveness, bronchitis, gastric ulcers, vascular damage caused by ischemic diseases and thrombosis, ischemic bowel diseases, inflammatory bowel diseases, necrotizing enterocolitis, intestinal lesions associated with thermal burns and leukotriene B4-mediated diseases, Coeliaz diseases, proctitis, eosinophilic gastroenteritis, mastocytosis, Crohn's disease, ulcerative colitis, migraine, rhinitis, eczema, interstitial nephritis, Good-pasture's syndrome, hemolytic-uremic syndrome, diabetic nephropathy, multiple myositis, Guillain-Barre syndrome, Meniere's disease, polyneuritis, multiple neuritis, mononeuritis, radiculopathy, hyperthroidism, Basedow's disease, pure red cell aplasia, aplastic anemia, hypoplastic anemia, idiopathic thrombocytopenic purpura, autoimmune hemolytic anemia, agranulocytosis, pernicious anemia, megaloblastic anemia, anerythroplasia, osteoporosis, sarcoidosis, fibroid lung, idiopathic interstitial pneumonia, dermatomyositis, leukoderma vulgaris, ichthyosis vulgaris, photoallergic sensitivity, cutaneous T cell lymphoma, arteriosclerosis, atherosclerosis, aortitis syndrome,

polyarteritis nodosa, myocardosis, scleroderma, Wegener's granuloma, Sjögren's syndrome, adiposis, eosinophilic fascitis, lesions of gingiva, periodontium, alveolar bone, substantia osses dentis, glomerulonephritis, male pattern alopecia or alopecia senilis by preventing epilation or providing hair germination and/or promoting hair generation and hair growth, muscular dystrophy; Pyoderma and Sezary's syndrome, Addison's disease, ischemia-reperfusion injury of organs which occurs upon preservation, transplantation or ischemic disease, endotoxin-shock, pseudomembranous colitis, colitis caused by drug or radiation, ischemic acute renal insufficiency, chronic renal insufficiency, toxinosis caused by lung-oxygen or drugs, lung cancer, pulmonary emphysema, cataracta, siderosis, retinitis, pigentosa, senile macular degeneration, vitreal scarring, corneal alkali burn, dermatitis erythema multiforme, linear IgA ballous dermatitis and cement dermatitis, gingivitis, periodontitis, sepsis, pancreatitis, diseases caused by environmental pollution, aging, carcinogenis, metastatis of carcinoma and hypobaropathy, disease caused by histamine or leukotriene-C4 release, Behcet's disease, autoimmune hepatitis, primary biliary cirrhosis sclerosing cholangitis, partial liver resection, acute liver necrosis, necrosis caused by toxin, viral hepatitis, shock, or anoxia, B-virus hepatitis, non-A/non-B hepatitis, cirrhosis, alcoholic cirrhosis, hepatic failure, fulminant hepatic failure, late-onset hepatic failure, "acute-on-chronic" liver failure, augention of chemotherapeutic effect, cytomegalovirus infection, HCMV infection, AIDS, cancer, senile dementia, trauma, and chronic bacterial infection.

[00321] The compounds of the present invention are suspected antiarrhythmic agents which are useful in the prevention and treatment (including partial alleviation or cure) of arrhythmias. As inhibitors of $K_v1.5$, compounds within the scope of the present invention are particularly useful in the selective prevention and treatment of supraventricular arrhythmias such as atrial fibrillation, and atrial flutter. By "selective prevention and treatment of supraventricular arrhythmias" is meant the prevention or treatment of supraventricular arrhythmias wherein the ratio of the prolongation of the atrial effective refractory period to the prolongation of the ventricular effective refractory period is greater than 1:1. This ratio can also be greater than 4:1, even greater than 10:1. In addition, the ratio may be such that

prolongation of the atrial effective refractory response period is achieved without significantly detectable prolongation of the ventricular effective refractory period.

[00322] In addition, the compounds within the scope of the present invention block I_{Kur}, and thus may be useful in the prevention and treatment of all I_{Kur}-associated conditions. An "I_{Kur}-associated condition" is a disorder which may be prevented, partially alleviated or cured by the administration of an I_{Kur} blocker. The $K_v1.5$ gene is known to be expressed in stomach tissue, intestinal/colon tissue, the pulmonary artery, and pancreatic beta cells. Thus, administration of an I_{Kur} blocker can provide useful treatment for disorders such as: reflux esauphagitis, functional dispepsia, constipation, asthma, and diabetes. Additionally, $K_v1.5$ is known to be expressed in the anterior pituitary. Thus, administration of an I_{Kur} blocker can stimulate growth hormone secretion. I_{Kur} inhibitors can additionally be useful in cell proliferative disorders such as leukemia, and autoimmune diseases such as rheumatoid arthritis and transplant rejection.

[00323] The present invention thus provides methods for the prevention or treatment of one or more of the aforementioned disorders, comprising the step of administering to a subject in need thereof an effective amount of at least one compound of the formula I, Ia, Ib, and/or Ic, preferably compounds exemplified in the examples, more preferably, Examples 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 and 137, even more preferably, Examples 7, 32, and 101, still even more preferably, Examples 7 and 101. Other therapeutic agents such as those described below may be employed with the inventive compounds in the present methods. In the methods of the present invention, such other therapeutic agent(s) may be administered prior to, simultaneously with or following the administration of the compound(s) of the present invention.

DOSAGE AND FORMULATION

[00324] The present invention also provides pharmaceutical compositions comprising at least one of the compounds of the formula I, Ia, Ib, and/or Ic, preferably compounds exemplified in the examples, more preferably, Examples 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 and 137, even more preferably, Examples 7, 32, and 101, still even more preferably, Examples 7 and 101,

or salts thereof capable of preventing or treating one or more of the aforementioned disorders in an amount effective therefor, and a pharmaceutically acceptable vehicle or diluent. The compositions of the present invention may contain other therapeutic agents as described below, and may be formulated, for example, by employing conventional solid or liquid vehicles or diluents, as well as pharmaceutical additives of a type appropriate to the mode of desired administration (for example, excipients, binders, preservatives, stabilizers, flavors, etc.) according to techniques such as those well known in the art of pharmaceutical formulation.

[00325] The compounds of the formula I, Ia, Ib, and/or Ic, preferably compounds exemplified in the examples, more preferably, Examples 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 and 137, even more preferably, Examples 7, 32, and 101, still even more preferably, Examples 7 and 101, may be administered by any suitable means, for example, orally, such as in the form of tablets, capsules, granules or powders; sublingually; bucally; parenterally, such as by subcutaneous, intravenous, intramuscular, or intrasternal injection or infusion techniques (*e.g.*, as sterile injectable aqueous or non aqueous solutions or suspensions); nasally such as by inhalation spray; topically, such as in the form of a cream or ointment; or rectally such as in the form of suppositories; in dosage unit formulations containing non toxic, pharmaceutically acceptable vehicles or diluents. The present compounds may, for example, be administered in a form suitable for immediate release or extended release. Immediate release or extended release may be achieved by the use of suitable pharmaceutical compositions comprising the present compounds, or, particularly in the case of extended release, by the use of devices such as subcutaneous implants or osmotic pumps. In the case where the compounds of formula I, Ia, Ib, and/or Ic, preferably compounds exemplified in the examples, more preferably, Examples 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 and 137, even more preferably, Examples 7, 32, and 101, still even more preferably, Examples 7 and 101, are being administered to prevent or treat arrhythmias, the compounds may be administered to achieve chemical conversion to normal sinus rhythm, or may optionally be used in conjunction with electrical cardioconversion.

[00326] Exemplary compositions for oral administration include suspensions which may contain, for example, microcrystalline cellulose for imparting bulk, alginic acid or sodium alginate as a suspending agent, methylcellulose as a viscosity enhancer, and sweeteners or flavoring agents such as those known in the art; and immediate release tablets which may contain, for example, microcrystalline cellulose, dicalcium phosphate, starch, magnesium stearate and/or lactose and/or other excipients, binders, extenders, disintegrants, diluents and lubricants such as those known in the art. The compounds of formula I, Ia, Ib, and/or Ic, preferably compounds exemplified in the examples, more preferably, Examples 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 and 137, even more preferably, Examples 7, 32, and 101, still even more preferably, Examples 7 and 101, may also be delivered through the oral cavity by sublingual and/or buccal administration. Molded tablets, compressed tablets or freeze-dried tablets are exemplary forms which may be used. Exemplary compositions include those formulating the present compound(s) with fast dissolving diluents such as mannitol, lactose, sucrose and/or cyclodextrins. Also included in such formulations may be high molecular weight excipients such as celluloses (AVICEL®) or polyethylene glycols (PEG). Such formulations may also include an excipient to aid mucosal adhesion such as hydroxy propyl cellulose (HPC), hydroxy propyl methyl cellulose (HPMC), sodium carboxy methyl cellulose (SCMC), maleic anhydride copolymer (*e.g.*, Gantrez), and agents to control release such as polyacrylic copolymer (*e.g.*, Carbopol 934). Lubricants, glidants, flavors, coloring agents and stabilizers may also be added for ease of fabrication and use.

[00327] Exemplary compositions for nasal aerosol or inhalation administration include solutions in saline which may contain, for example, benzyl alcohol or other suitable preservatives, absorption promoters to enhance bioavailability, and/or other solubilizing or dispersing agents such as those known in the art.

[00328] Exemplary compositions for parenteral administration include injectable solutions or suspensions which may contain, for example, suitable non toxic, parenterally acceptable diluents or solvents, such as mannitol, 1,3 butanediol, water, Ringer's solution, an isotonic sodium chloride solution, or other suitable dispersing or

wetting and suspending agents, including synthetic mono- or diglycerides, and fatty acids, including oleic acid.

[00329] Exemplary compositions for rectal administration include suppositories which may contain, for example, a suitable non irritating excipient, such as cocoa butter, synthetic glyceride esters or polyethylene glycols, which are solid at ordinary temperatures, but liquefy and/or dissolve in the rectal cavity to release the drug.

[00330] Exemplary compositions for topical administration include a topical carrier such as Plastibase (mineral oil gelled with polyethylene).

[00331] The effective amount of a compound of the present invention may be determined by one of ordinary skill in the art, and includes exemplary dosage amounts for an adult human of from about 0.001 to 100 mg/kg of body weight of active compound per day, which may be administered in a single dose or in the form of individual divided doses, such as from 1 to 4 times per day. It will be understood that the specific dose level and frequency of dosage for any particular subject may be varied and will depend upon a variety of factors including the activity of the specific compound employed, the metabolic stability and length of action of that compound, the species, age, body weight, general health, sex and diet of the subject, the mode and time of administration, rate of excretion, drug combination, and severity of the particular condition. Preferred subjects for treatment include animals, most preferably mammalian species such as humans, and domestic animals such as dogs, cats and the like, subject to the aforementioned disorders.

[00332] The compounds of the present invention may be employed alone or in combination with each other and/or other suitable therapeutic agents useful in the treatment of the aforementioned disorders or other disorders, including: other antiarrhythmic agents such as Class I agents (*e.g.*, propafenone), Class II agents (*e.g.*, carvadiol and propranolol), Class III agents (*e.g.*, sotalol, dofetilide, amiodarone, azimilide and ibutilide), Class IV agents (*e.g.*, diltiazem and verapamil), 5HT antagonists (*e.g.*, sulamserod, serraline and tropsetron), and dronedarone; calcium channel blockers (both L-type and T-type) such as diltiazem, verapamil, nifedipine, amlodipine and mybefradil; Cyclooxygenase inhibitors (*i.e.*, COX-1 and/or COX-2 inhibitors) such as aspirin, indomethacin, ibuprofen, piroxicam, naproxen, CELEBREX®, VIOXX® and NSAIDs; anti-platelet agents such as GPIIb/IIIa

blockers (*e.g.*, abciximab, eptifibatide and tirofiban), P2Y12 antagonists (*e.g.*, clopidogrel, cangrelor, ticlopidine and CS-747), P2Y1 antagonists, thromboxane receptor antagonists (*e.g.*, ifetroban), aspirin, and PDE-III inhibitors (*e.g.*, dipyridamole) with or without aspirin; diuretics such as chlorothiazide, hydrochlorothiazide, flumethiazide, hydroflumethiazide, bendroflumethiazide, methylchlorothiazide, trichloromethiazide, polythiazide, benzthiazide, ethacrynic acid tricrynafen, chlorthalidone, furosemide, musolimine, bumetanide, triamtrenene, amiloride, and spironolactone; anti-hypertensive agents such as alpha adrenergic blockers, beta adrenergic blockers, calcium channel blockers, diuretics, renin inhibitors, ACE inhibitors, (*e.g.*, captropril, zofenopril, fosinopril, enalapril, ceranopril, cilazopril, delapril, pentopril, quinapril, ramipril, lisinopril), A II antagonists (*e.g.*, losartan, irbesartan, valsartan), ET antagonists (*e.g.*, sitaxsentan, atrsentan and compounds disclosed in U.S. Patent Nos. 5,612,359 and 6,043,265), Dual ET/AII antagonist (*e.g.*, compounds disclosed in WO 00/01389), neutral endopeptidase (NEP) inhibitors, vasopepsidase inhibitors (dual NEP-ACE inhibitors) (*e.g.*, omapatrilat and gemopatrilat), nitrates, and combinations of such anti-hypertensive agents; antithrombotic/thrombolytic agents such as tissue plasminogen activator (tPA), recombinant tPA, tenecteplase (TNK), lanoteplase (nPA), factor VIIa inhibitors, factor Xa inhibitors (such as razaxaban), XIa inhibitors, thromin inhibitors (*e.g.*, hirudin and argatroban), PAI-1 inhibitors (*i.e.*, inactivators of tissue plasminogen activator inhibitors), α2-antiplasmin inhibitors, streptokinase, urokinase, prourokinase, anisoylated plasminogen streptokinase activator complex, and animal or salivary gland plasminogen activators; anticoagulants such as warfarin and heparins (including unfractionated and low molecular weight heparins such as enoxaparin and dalteparin); HMG-CoA reductase inhibitors such as pravastatin lovastatin, atorvastatin, simvastatin, NK-104 (a.k.a. itavastatin, or nisvastatin or nisbastatin) and ZD-4522 (a.k.a. rosuvastatin, or atavastatin or visastatin); other cholesterol/lipid lowering agents such as squalene synthetase inhibitors, fibrates, and bile acid sequestrants (*e.g.*, QUESTRAN®); antipoliferative agents such as cyclosporin A, TAXOL®, FK 506, and adriamycin; antitumor agents such as TAXOL®, adriamycin, epothilones, cisplatin and carboplatin; anti-diabetic agents such as biguanides (*e.g.*, metformin), glucosidase inhibitors (*e.g.*, acarbose), insulins,

meglitinides (*e.g.*, repaglinide), sulfonylureas (*e.g.*, glimepiride, glyburide and glipizide), biguanide/glyburide combinations (*i.e.*, GLUCOVANCE®), thiozolidinediones (*e.g.*, troglitazone, rosiglitazone and pioglitazone), PPAR-gamma agonists, aP2 inhibitors, and DP4 inhibitors; thyroid mimetics (including thyroid receptor antagonists) (*e.g.*, thyrotropin, polythyroid, KB-130015, and dronedarone); Mineralocorticoid receptor antagonists such as spironolactone and eplerinone; growth hormone secretagogues; anti-osteoporosis agents (*e.g.*, alendronate and raloxifene); hormone replacement therapy agents such as estrogen (including conjugated estrogens in premarin), and estradiol; antidepressants such as nefazodone and sertraline; antianxiety agents such as diazepam, lorazepam, buspirone, and hydroxyzine pamoate; oral contraceptives; anti-ulcer and gastroesophageal reflux disease agents such as famotidine, ranitidine, and omeprazole; anti-obesity agents such as orlistat; cardiac glycosides including digitalis and ouabain; phosphodiesterase inhibitors including PDE III inhibitors (*e.g.*, cilostazol), and PDE V inhibitors (*e.g.*, sildenafil); protein tyrosine kinase inhibitors; steroidal anti-inflammatory agents such as prednisone, and dexamethasone; and other anti-inflammatory agents such as ENBREL®. The combinations can be co-formulated or in the form of kits packaged to provide appropriate dosages for co-administration.

[00333] The above other therapeutic agents, when employed in combination with the compounds of the present invention, may be used, for example, in those amounts indicated in the Physicians' Desk Reference (PDR) or as otherwise determined by one of ordinary skill in the art.

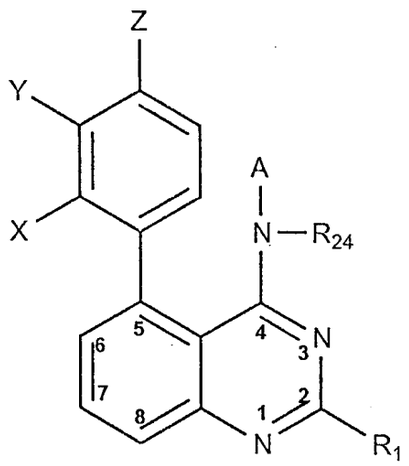
[00334] Publications and references, including but not limited to patents and patent applications, cited in this specification are herein incorporated by reference in their entirety in the entire portion cited as if each individual publication or reference were specifically and individually indicated to be incorporated by reference herein as being fully set forth. Any patent application to which this application claims priority is also incorporated by reference herein in the manner described above for publications and references.

[00335] While this invention has been described with an emphasis upon particular embodiments, it will be obvious to those of ordinary skill in the art that variations in the particular compounds and methods may be used and that it is intended that the

invention may be practiced otherwise than as specifically described herein. Accordingly, this invention includes all modifications encompassed within the spirit and scope of the invention as defined by the claims that follow.

WHAT IS CLAIMED IS:

1. A compound of formula I



I

or an enantiomer, diastereomer, tautomer, or salt thereof wherein:

X is H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CN, -NO_2, -$NR_{11}SO_2R_{12}$, -$SO_2NR_{11}R_{12}$, -$CONR_{11}R_{12}$, -$NR_{11}CONR_{11}R_{12}$, -$NCOR_{11}$, -$NR_{11}SO_2NR_{11}R_{12}$, -$OCONR_{11}R_{12}$, -CO_2R_{11} or -$NR_{11}R_{12}$;

Y is H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CN, -NO_2, -$SO_2NR_{11}R_{12}$, -$CONR_{11}R_{12}$, -$NR_{11}CONR_{11}R_{12}$, -$NCOR_{11}$, -$NR_{11}SO_2NR_{11}R_{12}$, -$OCONR_{11}R_{12}$, -CO_2R_{11} or -$NR_{11}R_{12}$;

Z is H, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 6- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -NO_2, -$NR_{11}SO_2R_{12}$, -$SO_2NR_{11}R_{12}$, -$NR_{11}CONR_{11}R_{12}$, -$NCOR_{11}$, -$NR_{11}SO_2NR_{11}R_{12}$, -$OCONR_{11}R_{12}$, -CO_2R_{11} or -$NR_{11}R_{12}$;

A is -$(CH_2)_m$-R_2, -$CH(R_{25})(R_{26})$, –$CH(R_{26})$-CO_2-R_{2a} or –$(CH_2)_{n-1}$-NR_{25}-CO_2-R_{24};

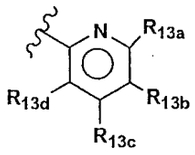
m is 0 to 4;

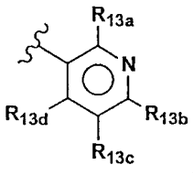
n is 1 to 4;

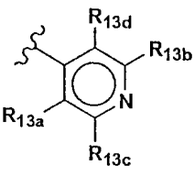
n-1 is 2 to 4;

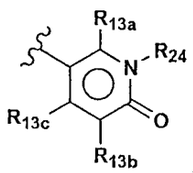
R_1 is -OH, F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{3-10} cycloalkyl, -CN, -$(CH_2)_n$-$SO_2NR_{11}R_{12}$, -$(CH_2)_n$-CO_2R_{11} or -$(CH_2)_n$-$NR_{11}SO_2R_{12}$, wherein the alkenyl and cycloalkyl may be optionally substituted with one or more R_{13}'s; or

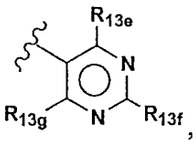
R_1 is selected from the group consisting of:

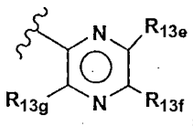


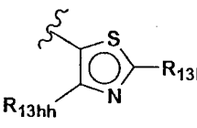


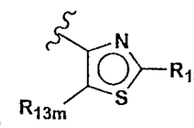


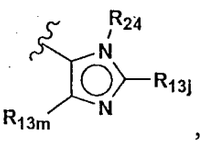


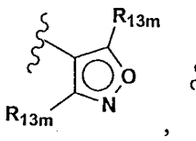


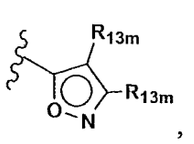


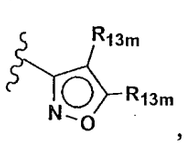


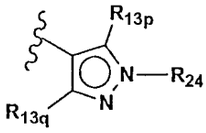


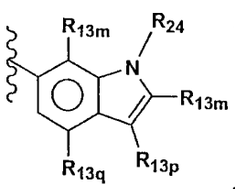


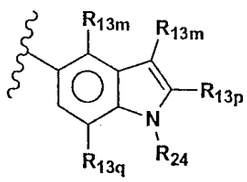


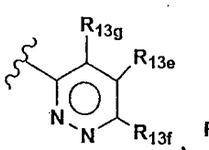


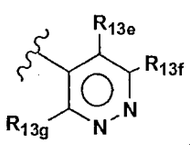


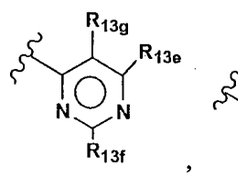


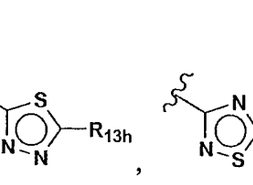


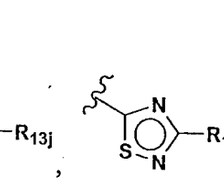


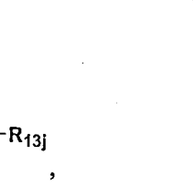


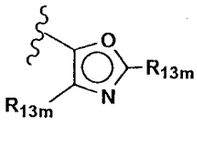


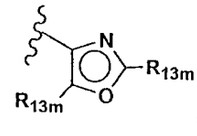


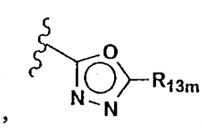


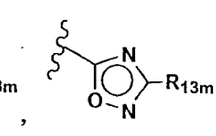


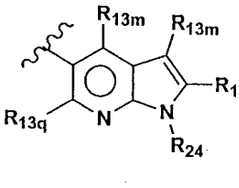


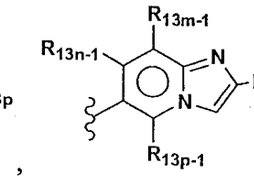


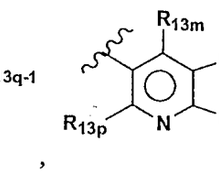


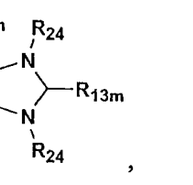


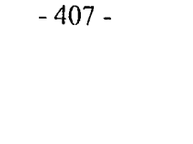








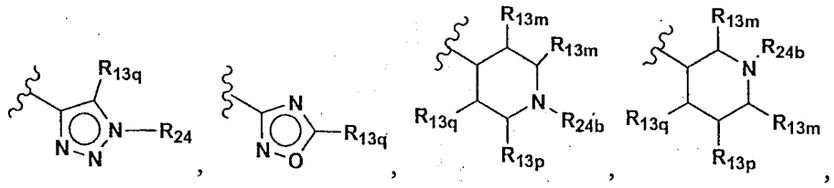


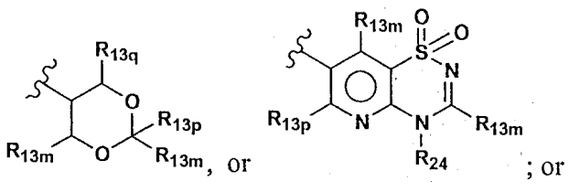




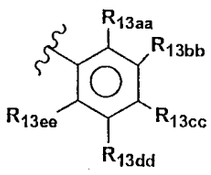






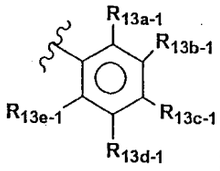


; or



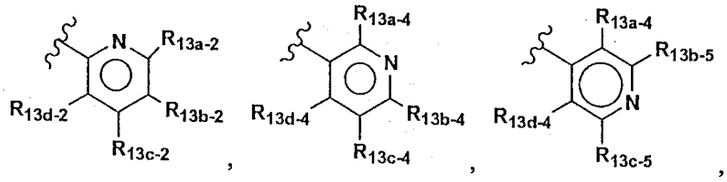
R_1 is ;

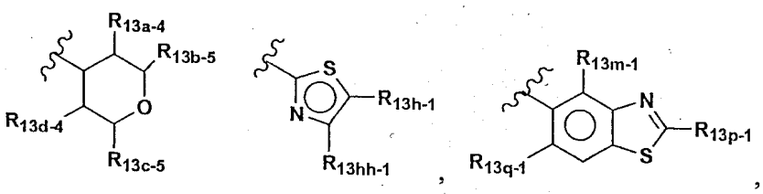
R_2 is C_{1-10} alkyl, cyclopropyl optionally substituted with one or more R_{13}'s; C_{4-10} cycloalkyl optionally substituted with one or more R_{13bb}'s; C_{3-10} cycloalkenyl optionally substituted with one or more R_{13b}'s; or $-NR_{14}R_{14}$; provided that R_2 is not $-NR_{14}R_{14}$ when m is 0, 1 or 3; or

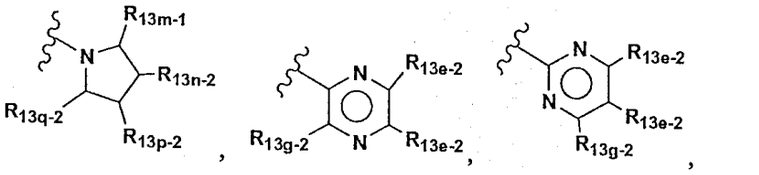


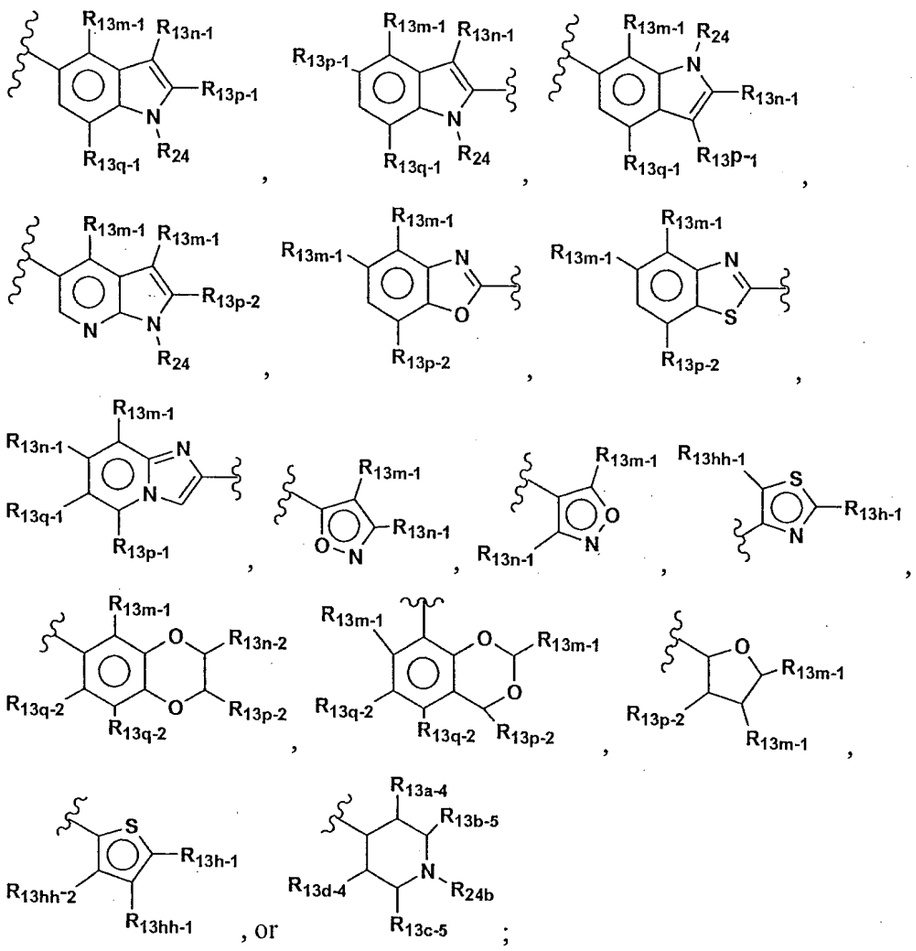
R_2 is ; or

R_2 is selected from the group consisting of:









R_{2a} is C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, $-NR_{14}R_{14}$, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, any of which is optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{11} and R_{12}, at each occurrence, are independently selected from H, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl and a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

R_{11} and R_{12} are taken together with the nitrogen to which they are attached to form a 4- to 12-membered heterocyclyl, wherein the heterocyclyl may be optionally substituted with one or more R_{13}'s and the heterocyclyl consists of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; provided that when R_{13} is alkyl substituted with one R_{14a}, R_{14a} is not –OH;

R_{13a}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13aa}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, -

$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2}, at each occurrence, is independently H, -OH, F, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-

membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13bb}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a

4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-(CH_2)_n-OCONR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13cc}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$, or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with

one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 6- to 12-membered heteroaryl, a 6- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, $-NO_2$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-NR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-4}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with

one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13dd}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl,

alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -

$C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13ee}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-1}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, -

$NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13f}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, -

$NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13h}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13h-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{7-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, -

$CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-

membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13j}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13m}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, –$CONR_{14}OR_{14}$ or –$NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13m-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a

4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13n-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with

one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ or $-NCOR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{14}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more

R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, -NO_2, -CO_2R_{26}, -$CO_2NR_{24}R_{24}$, -OCF_3, -OR_{25}, =O, -$CONR_{24}R_{24}$, -COR_{24}, -SO_2R_{24}, -$NR_{24}R_{24}$, -$NR_{24}CO_2R_{24}$, -$SO_2NR_{24}R_{24}$, or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{24}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, -NO_2, -CO_2R_{25}, -OCF_3, -OR_{25}, =O, -$CONR_{25}R_{25}$, -COR_{25}, -$NR_{25}R_{25}$, -$NR_{25}CO_2R_{25}$, or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24b}, at each occurrence, is independently selected from C_{1-10} alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CO_2R_{25}, -$SO_2NR_{25}R_{25}$, -COR_{25} or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered

heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

provide that:

(i) R_1 is not Cl when m is 0, 1 or 2; R_{13a-1} is H, $-CF_3$, or methoxy; R_{13c-1} is H, OH, methoxy or dimethylamino; X, Y, Z, R_{13b-1}, R_{13d-1}, R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d-2}, R_{13e-2}, R_{13g-2}, R_{13a-4}, R_{13b-4}, R_{13c-4}, R_{13d-4}, R_{13b-5}, R_{13c-5}, R_{13m-1}, R_{13n-1}, R_{13p-1}, and R_{13q-1} are H; and

(ii) m is not 0 or 1 when X, Y, R_{13a}, R_{13d}, R_{13e}, R_{13g}, R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d-2}, R_{13a-4}, R_{13b-4}, R_{13c-4}, R_{13d-4} R_{13b-5}, R_{13c-5}, R_{13h-1} and $R_{13hh-1}$are H; R_{13b} is H or $-SO_2NH_2$; R_{13c} is H, $-CONH_2$, $-SO_2N(C_2H_4OH)_2$, $-SO_2NHCOCH_3$, $-SO_2NH_2$, –tetrazolyl or (4-aminopiperidinyl)sulfonyl; R_{13f} is H or $-NHC_2H_4OCH_3$; and Z is H, $-CO_2H$, or $-CO_2CH_3$.

2. The compound, enantiomer, diastereomer, tautomer, or salt thereof, of claim 1, wherein:

X is H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CN, $-NO_2$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

Y is H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CN, $-NO_2$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

Z is H, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 6- to 12-membered heteroaryl, 4- to 12-membered

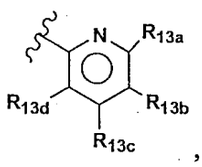
heterocyclyl, $-NO_2$, $-SO_2NR_{11}R_{12}$, $-NCOR_{11}$, $-NR_{11}SO_2NR_{11}R_{12}$, $-OCONR_{11}R_{12}$ or $-NR_{11}R_{12}$;

A is $-(CH_2)_m-R_2$, $-CH(R_{25})(R_{26})$ or $-CH(R_{26})-CO_2-R_{2a}$;

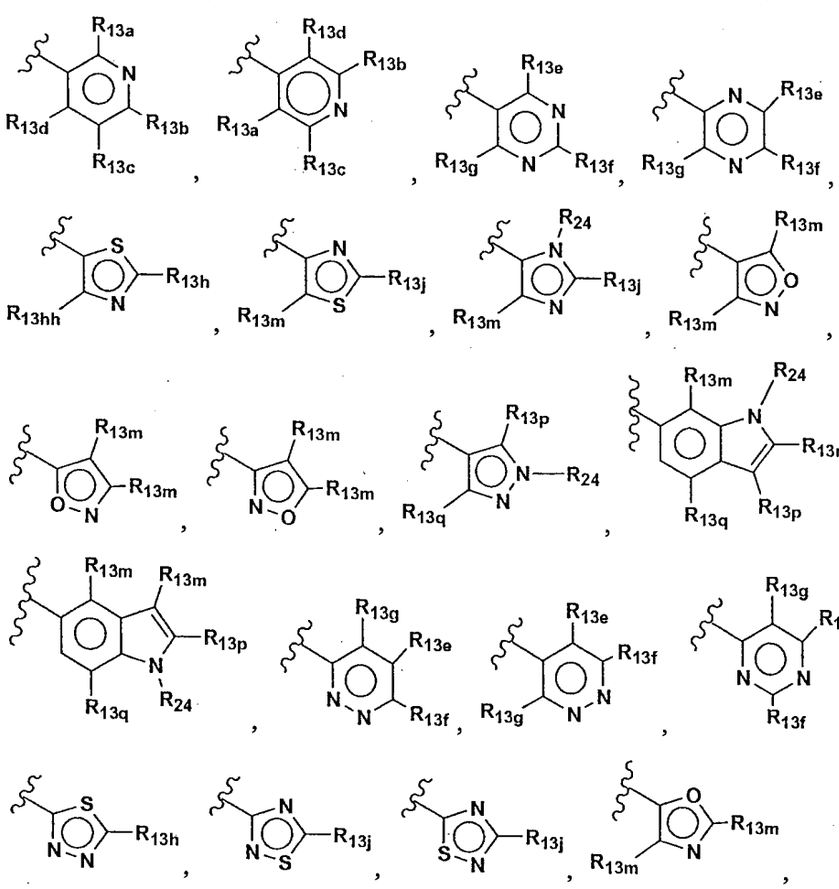
m is 0 to 4;

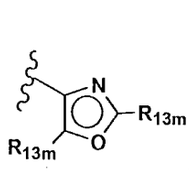
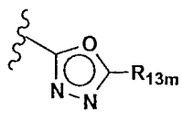
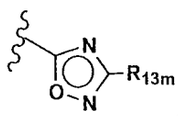
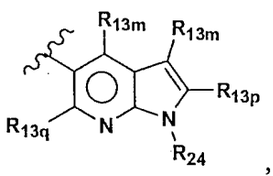
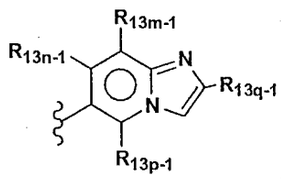
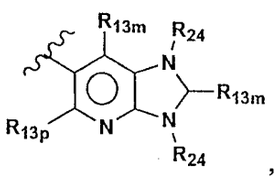
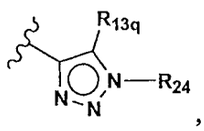
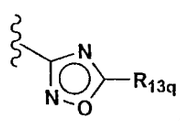
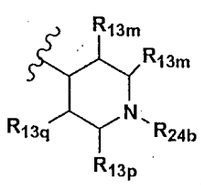
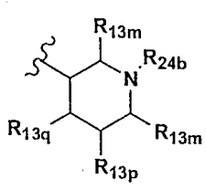
n is 1 to 4;

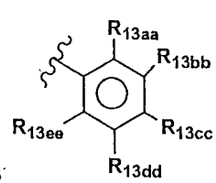
R_1 is -OH, F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{3-10} cycloalkyl, -CN, $-(CH_2)_n-SO_2NR_{11}R_{12}$ or $-(CH_2)_n-NR_{11}SO_2R_{12}$, wherein the alkenyl and cycloalkyl may be optionally substituted with one or more R_{13}'s; or



R_1 is selected from the group consisting of:

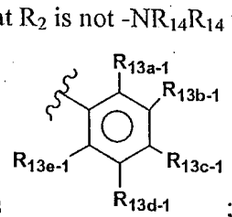











, or

; or



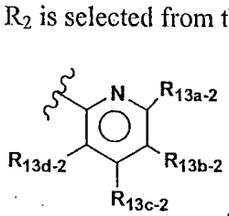
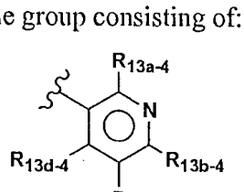
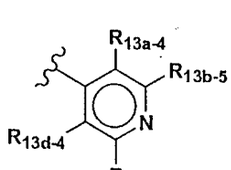
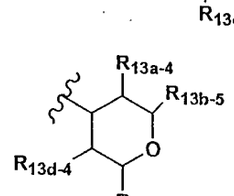
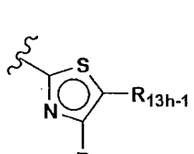
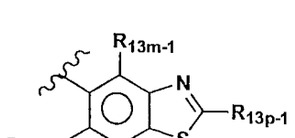
R_1 is ;

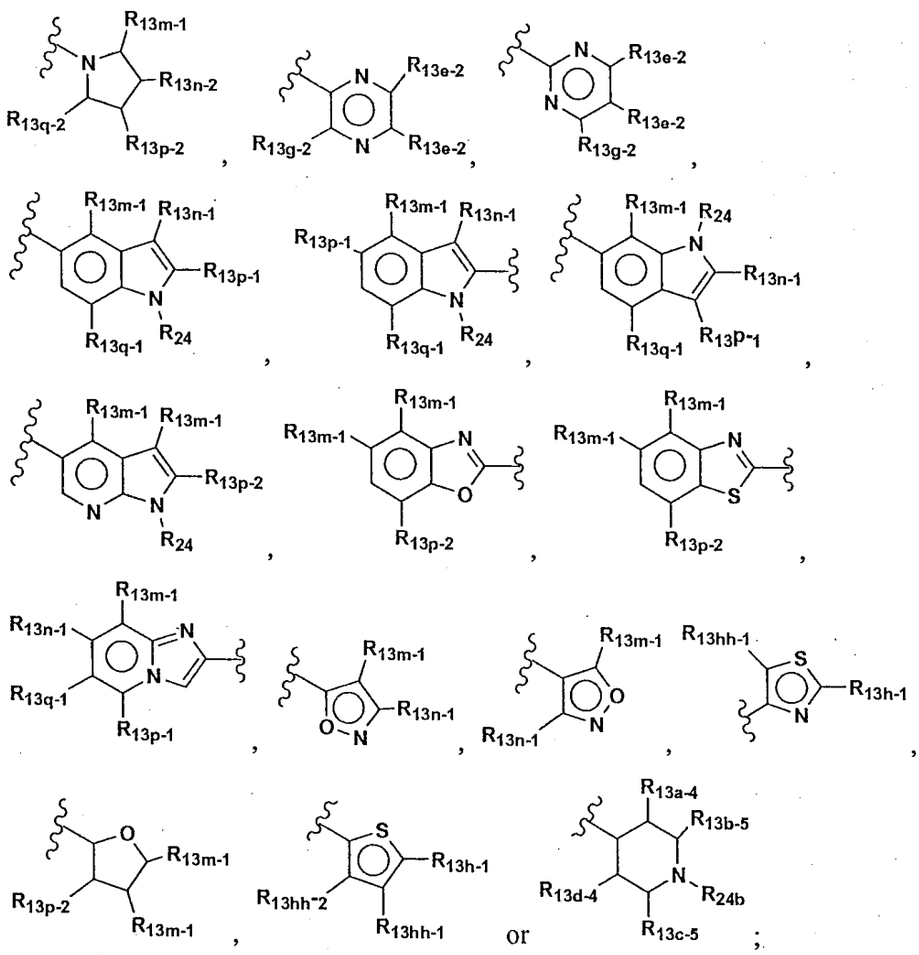
R_2 is $C_{1\text{-}10}$ alkyl, cyclopropyl optionally substituted with one or more R_{13}'s; $C_{4\text{-}10}$ cycloalkyl optionally substituted with one or more R_{13bb}'s; or $-NR_{14}R_{14}$; provided that R_2 is not $-NR_{14}R_{14}$ when m is 0, 1 or 3; or



R_2 is ; or

R_2 is selected from the group consisting of:



R_{2a} is C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, $-NR_{14}R_{14}$, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, any of which is optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{11} and R_{12}, at each occurrence, are independently selected from H, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl and a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

R_{11} and R_{12} are taken together with the nitrogen to which they are attached to form a 4- to 12-membered heterocyclyl, wherein the heterocyclyl may be optionally substituted with one or more R_{13}'s and the heterocyclyl consists of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; provided that when R_{13} is alkyl substituted with one R_{14a}, R_{14a} is not –OH;

R_{13a}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13aa}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -

$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

$R_{13a\text{-}1}$, at each occurrence, is independently H, -OH, F, Cl, Br, I, $C_{1\text{-}10}$ alkyl, $C_{1\text{-}10}$ alkoxy, halo$C_{1\text{-}10}$ alkyl, $C_{3\text{-}10}$ cycloalkyl, $C_{2\text{-}12}$ alkenyl, $C_{2\text{-}12}$ alkynyl, $C_{6\text{-}10}$aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-$C_{1\text{-}10}$ alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

$R_{13a\text{-}2}$, at each occurrence, is independently H, -OH, F, Br, I, $C_{1\text{-}10}$ alkyl, $C_{1\text{-}10}$ alkoxy, halo$C_{1\text{-}10}$ alkyl, $C_{3\text{-}10}$ cycloalkyl, $C_{2\text{-}12}$ alkenyl, $C_{2\text{-}12}$ alkynyl, $C_{6\text{-}10}$aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-$C_{1\text{-}10}$ alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

$R_{13a\text{-}4}$, at each occurrence, is independently H, -OH, F, Cl, Br, I, $C_{1\text{-}10}$ alkyl, $C_{1\text{-}10}$ alkoxy, halo$C_{1\text{-}10}$ alkyl, $C_{3\text{-}10}$ cycloalkyl, $C_{2\text{-}12}$ alkenyl, $C_{2\text{-}12}$ alkynyl, $C_{6\text{-}10}$aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-

membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13bb}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a

4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13cc}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 6- to 12-membered heteroaryl, a 6- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, $-NO_2$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-4}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13dd}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl

and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and

heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13ee}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-1}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the

alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13f}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$,

$-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13h}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13h-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{7-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$,

$-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, -

$CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13j}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13m}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13m-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-

membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13n-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a

4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{14}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, -NO_2, -CO_2R_{26}, -$OCONR_{24}R_{24}$, -$CO_2NR_{24}R_{24}$, -OCF_3, -OR_{25}, -$CONR_{24}R_{24}$, -COR_{24}, -SO_2R_{24}, -$NR_{24}R_{24}$, -$NR_{24}CO_2R_{24}$, -$SO_2NR_{24}R_{24}$, or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{24}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, -NO_2, -CO_2R_{25}, -OCF_3, -OR_{25}, -$CONR_{25}R_{25}$, -COR_{25}, -$NR_{25}R_{25}$, -$NR_{25}CO_2R_{25}$, or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24b}, at each occurrence, is independently selected from C_{1-10} alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CO_2R_{25}, -$SO_2NR_{25}R_{25}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1,

2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

3. The compound, enantiomer, diastereomer, tautomer, or salt thereof, of claim 1, wherein:

X is H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CN, $-NO_2$, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

Y is H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, -CN, $-NO_2$, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

Z is H, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, a 6- to 12-membered heteroaryl, 4- to 12-membered heterocyclyl, $-NO_2$ or $-NR_{11}R_{12}$;

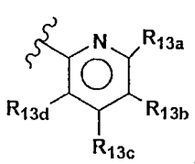
A is $-(CH_2)_m-R_2$ or $-CH(R_{25})(R_{26})$;

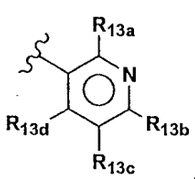
m is 0 to 4;

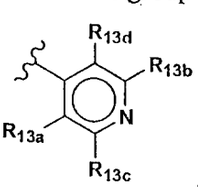
n is 1 to 4;

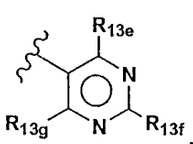
R_1 is F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{2-12} alkenyl, C_{3-10} cycloalkyl, $-(CH_2)_n-SO_2NR_{11}R_{12}$ or $-(CH_2)_n-NR_{11}SO_2R_{12}$, wherein the alkenyl and cycloalkyl may be optionally substituted with one or more R_{13}'s; or

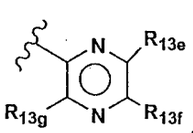
R_1 is selected from the group consisting of:

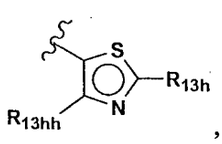
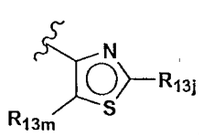
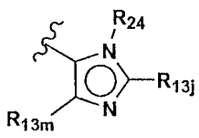
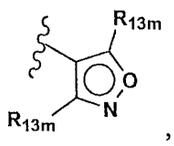
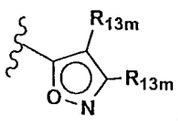
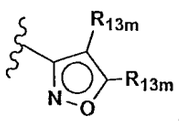
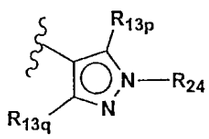
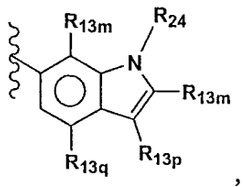
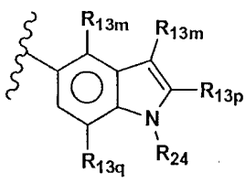
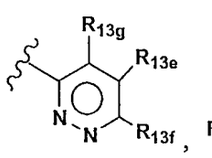
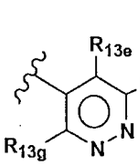
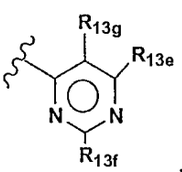
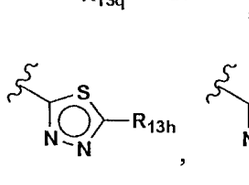
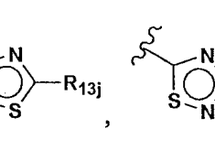
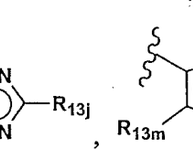
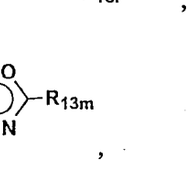
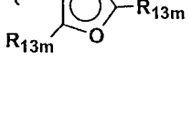
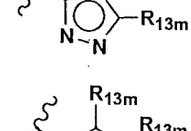
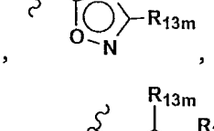
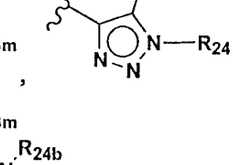
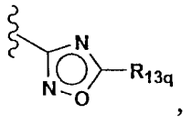
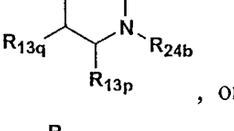
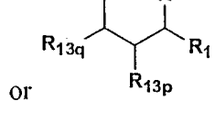
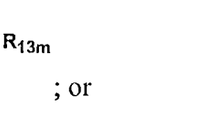
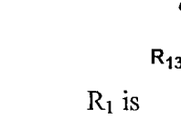
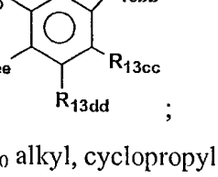
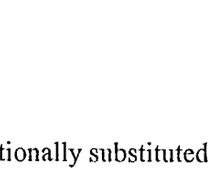


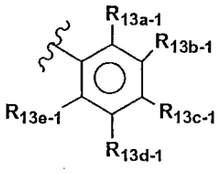


































, or

; or

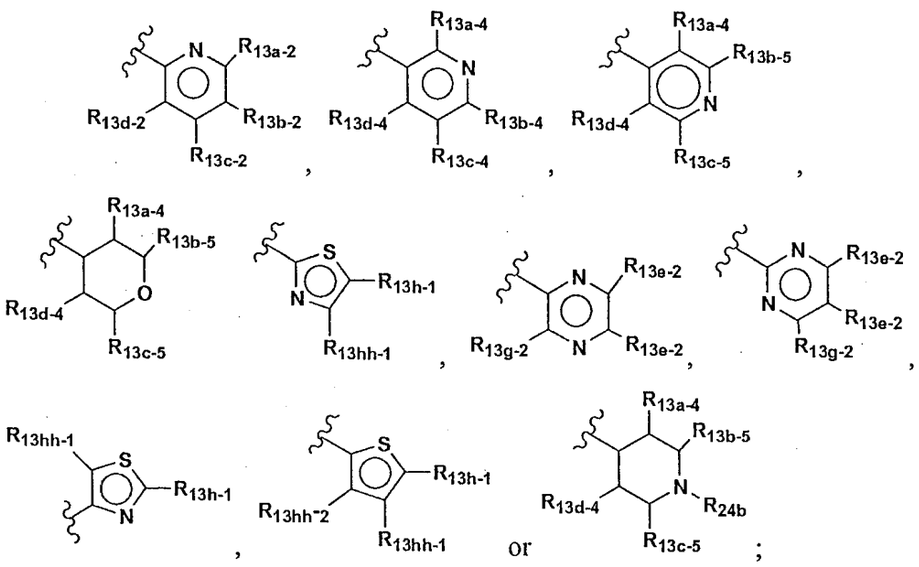


R_1 is ;

R_2 is $C_{1\text{-}10}$ alkyl, cyclopropyl optionally substituted with one or more R_{13}'s; or $C_{4\text{-}10}$ cycloalkyl optionally substituted with one or more R_{13bb}'s; or

R_2 is ; or

R_2 is selected from the group consisting of:



R_{11} and R_{12}, at each occurrence, are independently selected from H, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl and a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

R_{11} and R_{12} are taken together with the nitrogen to which they are attached to form a 4- to 12-membered heterocyclyl, wherein the heterocyclyl may be optionally substituted with one or more R_{13}'s and the heterocyclyl consists of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl

and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; provided that when R_{13} is alkyl substituted with one R_{14a}, R_{14a} is not –OH;

R_{13a}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13aa}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

$R_{13a\text{-}1}$, at each occurrence, is independently -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, or –$CONR_{14}OR_{14}$, wherein the

alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2}, at each occurrence, is independently H, -OH, F, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, -

$NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13bb}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, -

$CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$,

$-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13cc}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 6- to 12-membered heteroaryl, a 6- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, $-NO_2$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$,

$-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-4}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, -

$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13dd}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered

heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13ee}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4-

to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-1}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13f}, at each occurrence, is independently -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl

and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13h}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

$R_{13h\text{-}1}$, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{7-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and

heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13hh-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13j}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or –

$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13m}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13p}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13q}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$,

$-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ or $-CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{14}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, $-NO_2$, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-CONR_{24}R_{24}$, $-COR_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$, $-NR_{24}CO_2R_{24}$, $-SO_2NR_{24}R_{24}$, or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{24}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, -NO_2, -CO_2R_{25}, -OCF_3, -OR_{25}, -$CONR_{25}R_{25}$, -COR_{25}, -$NR_{25}CO_2R_{25}$, or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24b}, at each occurrence, is independently selected from C_{1-10} alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CO_2R_{25}, -$SO_2NR_{25}R_{25}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

4. The compound, enantiomer, diastereomer, tautomer, or salt thereof, of claim 1, wherein:

X is H, F, Cl, Br, I, C_{1-10} alkoxy, haloC_{1-10} alkyl, 4- to 12-membered heterocyclyl, -CO_2R_{11} or -$NR_{11}R_{12}$;

Y is H, F, Cl, Br, I, C_{1-10} alkoxy, haloC_{1-10} alkyl, 4- to 12-membered heterocyclyl, -CO_2R_{11} or -$NR_{11}R_{12}$;

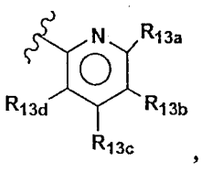
Z is H, Cl, Br, I, C_{1-10} alkoxy, haloC_{1-10} alkyl, 4- to 12-membered heterocyclyl or -$NR_{11}R_{12}$;

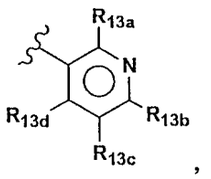
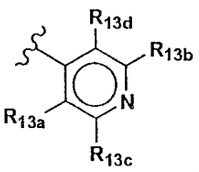
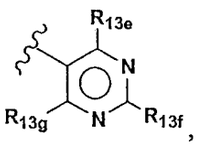
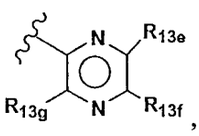
A is -$(CH_2)_m$-R_2;

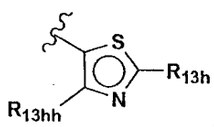
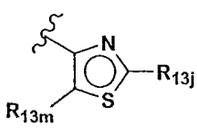
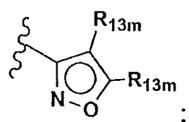
m is 0 to 3;

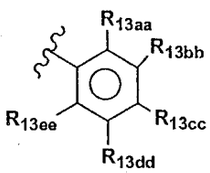
n is 1 to 3;

R_1 is Cl, C_{2-12} alkenyl, C_{3-10} cycloalkyl, wherein the alkenyl and cycloalkyl may be optionally substituted with one or more R_{13}'s; or

R_1 is selected from the group consisting of:  ,

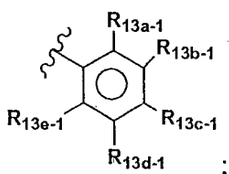
 ,  ,  ,  ,

 ,  or  ; or



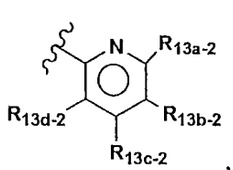
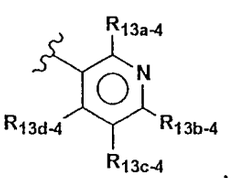
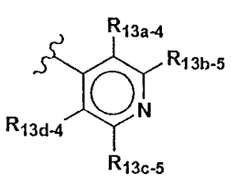
R_1 is ;

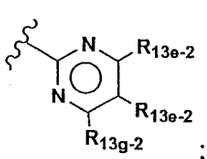
R_2 is cyclopropyl optionally substituted with one or more R_{13}'s; or



R_2 is ; or

R_2 is selected from the group consisting of:

 ,  ,  or

 ;

R_{11} and R_{12}, at each occurrence, are independently selected from H, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl and

a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; provided that when R_{13} is alkyl substituted with one R_{14a}, R_{14a} is not –OH;

R_{13a}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13aa}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl,

cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, or –$CONR_{14}OR_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2}, at each occurrence, is independently H, -OH, F, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl,

cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13bb}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted

with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of

carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -CO_2R_{26} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13cc}, at each occurrence, is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 6- to 12-membered heteroaryl, a 6- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-4}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-5}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13dd}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-1}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$ or -CO_2R_{14}, wherein the alkyl, cycloalkyl, alkenyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-4}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13ee}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-1}, at each occurrence, is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{2-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13e-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13f}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13g-2}, at each occurrence, is independently H, -OH, F, Cl, Br, I, C_{2-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-CONR_{24}R_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

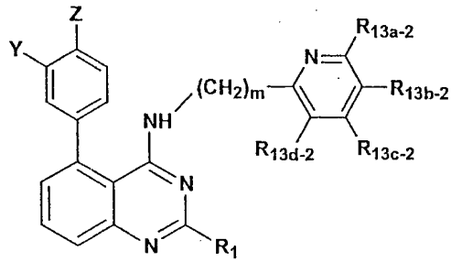
R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon

atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

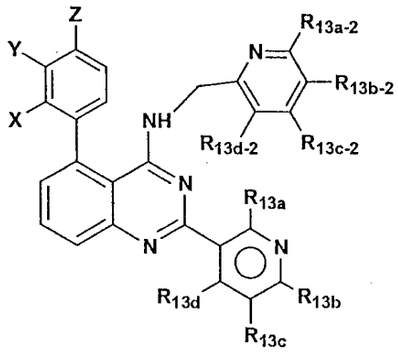
5. The compound, enantiomer, diastereomer, tautomer, or salt thereof, of claim 1, wherein the compound is a compound of formula (Ia):



(Ia)

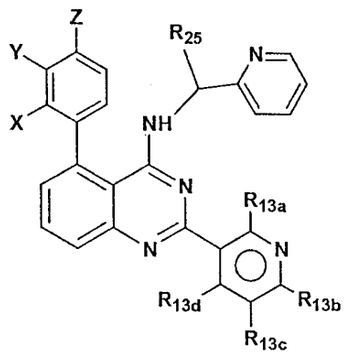
and m, Y, Z, R_1, R_{13a-2}, R_{13b-2}, R_{13c-2} and R_{13d-2} are as defined in claim 1.

6. A compound of formula (Ib) or (Ic):



Ib

or



Ic

or an enantiomer, diastereomer, tautomer, or salt thereof wherein:

X is H, F, Cl, Br, I, C_{1-10} alkoxy, haloC_{1-10} alkyl, 4- to 12-membered heterocyclyl, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

Y is H, F, Cl, Br, I, C_{1-10} alkoxy, haloC_{1-10} alkyl, 4- to 12-membered heterocyclyl, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

Z is H, Cl, Br, I, C_{1-10} alkoxy, haloC_{1-10} alkyl, 4- to 12-membered heterocyclyl or $-NR_{11}R_{12}$;

R_{11} and R_{12}, at each occurrence, are independently selected from H, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl and

a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2} is independently H, -OH, F, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b} is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$CONR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$ or -$NR_{14}CONR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl

and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c} is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, hydroxyC_{1-10} alkyl, cyanoC_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$(CH_2)_n$-$OCONR_{14}R_{14}$, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -CO_2R_{26}, -$NR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$ or -$NR_{14}CONR_{14}R_{14}$, wherein the cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, or 3 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2} is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, -CO_2H, -CO_2R_{26}, -$OCONR_{24}R_{24}$, -$CO_2NR_{24}R_{24}$, -OCF_3, -OR_{25}, -$CONR_{24}R_{24}$, -SO_2R_{24}, -$NR_{24}R_{24}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; or

two R_{24}'s are taken together with the atoms to which they are attached to form a cyclic ring, wherein the cyclic ring may be optionally substituted with one or more R_{24a}'s and optionally contain 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

provided that X, Y, Z, R_{13a}, R_{13b}, R_{13d}, R_{13a-2}, R_{13b-2}, R_{13c-2} and R_{13d-2} is not all H when R_{13c} is $-C(=O)N(C_2H_4OCH_3)_2$, $-SO_2N(C_2H_4OH)_2$.

7. The compound, enantiomer, diastereomer, tautomer, or salt thereof, of claim 6, wherein:

X is H, F, Cl, Br, I, C_{1-10} alkoxy, haloC_{1-10} alkyl, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

Y is H, F, Cl, Br, I, C_{1-10} alkoxy, haloC_{1-10} alkyl, $-CO_2R_{11}$ or $-NR_{11}R_{12}$;

Z is H, Cl, Br, I, C_{1-10} alkoxy, haloC_{1-10} alkyl or $-NR_{11}R_{12}$;

R_{11} and R_{12}, at each occurrence, are independently selected from H, C_{1-10} alkyl, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl and a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{13}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2} is independently H, -OH, F, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b} is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, or $-NR_{14}CONR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl,

alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c} is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, hydroxyC_{1-10} alkyl, cyanoC_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -CO_2R_{26}, -$NR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$ or -$NR_{14}CONR_{14}R_{14}$, wherein the cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2 or 3 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2} is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2} is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, -CO_2R_{26}, -$CO_2NR_{24}R_{24}$, -OCF_3, -OR_{25}, -$CONR_{24}R_{24}$, -SO_2R_{24}, -$NR_{24}R_{24}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

8. The compound, enantiomer, diastereomer, tautomer, or salt thereof, of claim 6, wherein:

X is H, F, Cl, Br, I, C_{1-10} alkoxy or haloC_{1-10} alkyl;

Y is H, F, Cl, Br, I, C_{1-10} alkoxy or haloC_{1-10} alkyl;

Z is H, Cl, Br, I, C_{1-10} alkoxy or haloC_{1-10} alkyl;

R_{13a} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m$-SO_2R_{14}, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m$-$NR_{14}SO_2R_{14}$, $-(CH_2)_n$-

$NR_{14}SO_2NR_{14}R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13a-2} is independently H, -OH, F, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b} is independently H, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, or $-NR_{14}CONR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13b-2} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-CO_2R_{14}$ or $-NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c} is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, hydroxyC_{1-10} alkyl, cyanoC_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, -

$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -$NR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$ or -$NR_{14}CONR_{14}R_{14}$, wherein the cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2 or 3 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13c-2} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d} is independently H, -OH, F, Cl, Br, I, C_{1-10} alkyl, C_{2-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{13d-2} is independently H, -OH, Cl, Br, I, C_{1-10} alkyl, C_{1-10} alkoxy, haloC_{1-10} alkyl, C_{3-10} cycloalkyl, C_{2-12} alkenyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, a 4- to 12-membered heteroaryl-C_{1-10} alkyl, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -CO_2R_{14} or -$NR_{14}R_{14}$, wherein the alkyl, cycloalkyl, alkenyl, alkoxy, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{14a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14} is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a} is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24} is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a} is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25} is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26} is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

9. The compound, enantiomer, diastereomer, tautomer, or salt thereof, of claim 6, wherein:

X, Y, Z, R_{13a}, R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d} and R_{13d-2} are H;

R_{13b}, at each occurrence, is independently H, C_{1-10} alkoxy, or $-NR_{14}R_{14}$;

R_{13c}, at each occurrence, is independently H, C_{1-10} alkyl, C_{3-10} cycloalkyl, a 4- to 12-membered heteroaryl, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-CONR_{14}R_{14}$ or $-NR_{14}R_{14}$, wherein the cycloalkyl, and heteroaryl may be optionally substituted with one or more R_{14a}'s and the heteroaryl consists of carbon atoms and 1, 2 or 3 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14}, at each occurrence, is independently selected from hydrogen, C_{1-10} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, a 4- to 12-membered heteroaryl or a 4- to 12-membered heterocyclyl, wherein the alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with be optionally substituted with 0-3 R_{14a} and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{14a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the alkyl, aryl, heteroaryl and heterocyclyl may be optionally substituted with one or more R_{24a}'s and the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{24a}, at each occurrence, is independently selected from F, Cl, Br, I, C_{1-10} alkyl, haloC_{1-10}alkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, a 4- to 12-membered heteroaryl, a 4- to 12-membered heterocyclyl, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ or C_{6-10}arylC_{1-10}alkyl, wherein the heteroaryl and heterocyclyl consist of carbon

atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O;

R_{25}, at each occurrence, is independently selected from hydrogen, C_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O; and

R_{26}, at each occurrence, is independently selected from C_{1-10}alkyl, haloC_{1-10}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, a 4- to 12-membered heteroaryl or 4- to 12-membered heterocyclyl, wherein the heteroaryl and heterocyclyl consist of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, S, or O.

10. A compound, enantiomer, diastereomer, or salt thereof, selected from the compounds set forth in the examples.

11. A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of any one of claims 1 to 10.

12. The pharmaceutical composition of claim 11, further comprising at least one other therapeutic agent.

13. A method of treating or preventing arrhythmia comprising administering to a patient in need thereof an effective amount of at least one compound of any one of claims 1 to 10.

14. A method of controlling heart rate comprising administering to a patient in need thereof an effective amount of at least one compound of any one of claims 1 to 10.

15. A method of treating an I_{Kur}-associated condition comprising administering to a patient in need thereof an effective amount of at least one compound of any one of claims 1 to 10.

TRADUCCION
SOLICITUD
INTERNACIONAL

QUINAZOLINAS COMO INHIBIDORES DE LOS CANALES IÓNICOS DE POTASIO

CAMPO DE LA INVENCIÓN

La presente invención proporciona quinazolinas útiles como inhibidores de la función del canal de potasio (especialmente inhibidores de la subfamilia K_v1 de los canales de K+ dependientes de voltaje, más especialmente inhibidores de los canales $K_v1.5$ (que se ha vinculado con la corriente I_{Kur} de K+ rectificadora tardía de activación ultrarrápida) y/o los canales $K_v1.3$ y/o los canales $K_v1.1$) y a composiciones farmacéuticas que contienen dichos compuestos. La presente invención además proporciona procedimientos para usar dichos compuestos en el tratamiento y la prevención de arritmias, trastornos asociados con la I_{Kur} y otros trastornos mediados por la función de los canales iónicos.

ANTECEDENTES DE LA INVENCIÓN

Se cree que la corriente de K+ rectificadora tardía de activación ultrarrápida ((I_{Kur}) representa el homólogo nativo de un canal de potasio clonado designado $K_v1.5$ y, aunque está presente en la auricular humana, parece estar ausente en el ventrículo humano. Además, dada la rapidez de su activación y la limitada inactivación lenta, se cree que la I_{Kur} contribuye significativamente a la repolarización en la aurícula humana. En consecuencia, un bloqueante específico de I_{Kur}, es decir un compuesto que bloquea $K_v1.5$, superaría el inconveniente de otros compuestos prolongando la refractariedad retardando la repolarización en la aurícula humana sin producir los retrasos en

la repolarización ventricular subyacentes a la arritmogenia tras despolarizaciones y el síndrome de QT largo adquirido observados durante el tratamiento con los agentes antiarrítmicos actuales de clase III. (Los agentes antiarrítmicos de clase III son fármacos que producen una prolongación selectiva de la duración del potencial de acción sin una depresión cardíaca significativa).

Se ha mostrado que existen anomalías inmunorreguladoras en una amplia variedad de enfermedades inflamatorias autoinmunitarias y crónicas, incluidas la eritematosis lúpica sistémica, la artritis reumatoide crónica, la diabetes mellitus de tipo I y de tipo II, la enfermedad intestinal inflamatoria, la cirrosis biliar, la uveítis, la esclerosis múltiple y otros trastornos tales como enfermedad de Crohn, colitis ulcerosa, penfigoide ampolloso, sarcoidosis, psoriasis, ictiosis, oftalmopatía de Graves y asma. Aunque las patogenias subyacentes de cada una de estas afecciones pueden variar, tienen en común la aparición de diversos autoanticuerpos y linfocitos autorreactivos. Tal autoreactividad puede deberse, en parte, a una pérdida de los controles homeostáticos bajo los cuales funciona el sistema inmunológico. De forma similar, tras un transplante de médula ósea o de un órgano, los linfocitos reconocen los antígenos de tejido extraño y comienzan a producir mediadores inmunitarios que conducen al rechazo del injerto o al rechazo de injerto contra huésped.

Un resultado final de un proceso autoinmunitario o de rechazo es la destrucción tisular producida por las células inflamatorias y los mediadores que liberan. Los agentes antiinflamatorios, como los AINE, actúan principalmente a través del bloqueo del efecto o de la secreción de estos mediadores, pero no

modifican la base inmunológica de la enfermedad. Por otro lado, los agentes citotóxicos, tales como la ciclofosfamida, actúan de un modo no específico mediante el que se cortan las respuestas tanto normal como autoinmunitaria. De hecho, los pacientes tratados con dichos agentes inmunosupresores no específicos tienen la misma probabilidad de sucumbir a la infección como a la enfermedad autoinmunitaria.

La ciclosporina A, aprobada por la FDA de EE.UU. en 1983, es, actualmente, el principal fármaco usado para prevenir el rechazo de órganos transplantados. En 1993, la FDA de EE.UU. aprobó el fármaco FK-506 (PROGRAF®) para la prevención del rechazo en el transplante de hígado. La ciclosporina A y el FK-506 actúan a través de la inhibición de la movilización por parte del sistema inmunológico del cuerpo de su extensor arsenal de agentes protectores naturales para rechazar la proteína extraña del transplante. En 1994, la FDA de EE.UU. aprobó la ciclosporina A para el tratamiento de la psoriasis grave y las agencias reguladoras europeas la han aprobado para el tratamiento de la dermatitis atópica. Aunque estos agentes son eficaces en la lucha contra el rechazo de los transplantes, se sabe que la ciclosporina A y el FK-506 producen varios efectos secundarios indeseados, incluidos nefrotoxicidad, neurotoxicidad y molestias gastrointestinales. Por tanto, todavía queda por desarrollar un inmunosupresor selectivo sin estos efectos secundarios. Los inhibidores de los canales de potasio, como se describen en el presente documento, son una solución prometedora a este problema, ya que, por ejemplo, los inhibidores de $K_v1.3$, son inmunosupresores. Véase Wulff y col., "Potassium channels as therapeutic targets for autoimmune disorders," *Curr. Opin. Drug Discov. Devel.*, 6(5):640-

647 (Sep. 2003); Shah y col., "Immunosuppressive effects of a $K_v1.3$ inhibitor," *Cell Immunol.*, 221(2):100-106 (Feb. 2003); Hanson y col., "UK-78,282, a novel piperidine compound that potently blocks the $K_v1.3$ voltage-gated potassium channel and inhibits human T cell activation," *Br. J. Pharmacol.*, 126(8):1707-1716 (Abr. 1999).

Los inhibidores de $K_v1.5$ y de otros canales $K_v1.x$ estimulan la motilidad gastrointestinal. Por tanto, se cree que los compuestos de la invención son útiles en el tratamiento de los trastornos de la motilidad, tales como la esofagitis por reflujo. Véase Frey y col., "Blocking of cloned and native delayed rectifier K channels from visceral smooth muscles by phencyclidine," *Neurogastroenterol. Motil.*, 12(6):509-516 (Dic. 2000); Hatton y col., "Functional and molecular expression of a voltage-dependent K(+) channel ($K_v1.1$) in interstitial cells of Cajal," *J. Physiol.*, 533(Pt 2):315-327 (Jun. 1, 2001); Vianna-Jorge y col., "Shaker-type K_v1 channel blockers increase the peristaltic activity of guinea-pig ileum by stimulating acetylcholine and tachykinins release by the enteric nervous system," *Br. J. Pharmacol.*, 138(1):57-62 (Jan. 2003); Koh y col., "Contribution of delayed rectifier potassium currents to the electrical activity of murine colonic smooth muscle," *J. Physiol.*, 515(Pt. 2):475-487 (Mar. 1, 1999).

Los inhibidores de $K_v1.5$ relajan el músculo liso de las arterias pulmonares. Por tanto, se cree que los compuestos de la invención son útiles en la hipertensión y, por otro lado, para mejorar la salud vascular. Véase Davies y col., "K_v channel subunit expression in rat pulmonary arteries," *Lung*, 179(3):147-161 (2001), Epub. Feb. 4, 2002; Pozeg y col., "*In vivo* gene transfer of the O2-sensitive potassium channel $K_v1.5$ reduces pulmonary hypertension

and restores hypoxic pulmonary vasoconstriction in chronically hypoxic rats," *Circulation*, 107(15):2037-2044 (Apr. 22, 2003), Epub. Abr. 14, 2003.

Los inhibidores de $K_v1.3$ incrementan la sensibilidad a la insulina. Por tanto, se cree que los compuestos de la invención son útiles en el tratamiento de la diabetes. Véase Xu y col., "The voltage-gated potassium channel $K_v1.3$ regulates peripheral insulin sensitivity," *Proc. Natl. Acad. Sci. U.S.A.*, 101(9):3112-3117 (Mar. 2, 2004), Epub. Feb. 23, 2004; MacDonald y col., "Members of the K_v1 and K_v2 voltage-dependent K(+) channel families regulate insulin secretion," *Mol. Endocrinol.*, 15(8):1423-1435 (Aug. 2001); MacDonald y col., "Voltage-dependent K(+) channels in pancreatic beta cells: role, regulation and potential as therapeutic targets," *Diabetologia*, 46(8):1046-1062 (Aug. 2003), Epub. Jun. 27, 2003.

Se cree que la estimulación de $K_v1.1$ reduce la actividad de las convulsiones mediante la hiperpolarización de neuronas. Por tanto, se cree que los compuestos de la invención son útiles en el tratamiento de las convulsiones, incluidas las convulsiones asociadas con la epilepsia y otras enfermedades neurológicas. Véase Rho y col., "Developmental seizure susceptibility of kv1.1 potassium channel knockout mice," *Dev. Neurosci.*, 21(3-5):320-327 (Nov. 1999); Coleman y col., "Subunit composition of K_v1 channels in human CNS," *J. Neurochem.*, 73(2):849-858 (Aug. 1999); Lopantsev y col., "Hyperexcitability of CA3 pyramidal cells in mice lacking the potassium channel subunit $K_v1.1$," *Epilepsia*, 44(12):1506-1512 (Dec. 2003); Wickenden, "Potassium channels as anti-epileptic drug targets," *Neuropharmacology*, 43(7):1055-1060 (Dic. 2002).

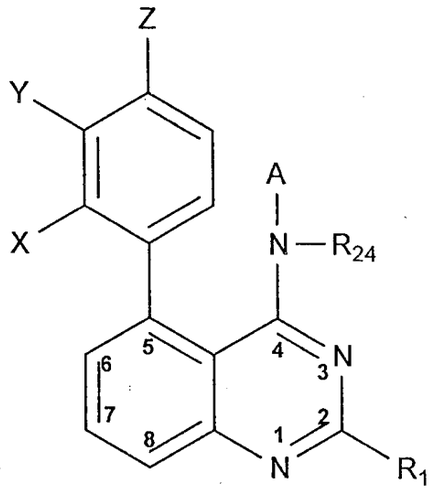
La inhibición de los canales $K_v1.x$ mejora la cognición en modelos

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animales. Por tanto, se cree que los compuestos de la invención son útiles en la mejora de la cognición y/o el tratamiento de trastornos cognitivos. Véase Cochran y col., "Regionally selective alterations in local cerebral glucose utilization evoked by charybdotoxin, a blocker of central voltage-activated K+-channels," *Eur. J. Neurosci.*, 14(9):1455-1463 (Nov. 2001); Kourrich y col., "Kaliotoxin, a $K_v1.1$ and $K_v1.3$ channel blocker, improves associative learning in rats," *Behav. Brain Res.*, 120(1):35-46 (Abr. 8, 2001).

RESUMEN DE LA INVENCIÓN

De acuerdo con la presente invención, se proporcionan compuestos acíclicos y compuestos relacionados que tienen la estructura general de fórmula I:



en la que A, X, Y, Z, R_1 y R_{24} se definen más adelante.

Mediante el uso de una cantidad eficaz correspondiente de al menos un compuesto descrito en la presente memoria descriptiva se proporcionan procedimientos para tratar (incluyendo mejorar) o prevenir arritmias, fibrilación

auricular, aleteo auricular, arritmias supraventriculares, trastornos gastrointestinales (tales como esofagitis por reflujo o un trastorno de la motilidad), enfermedad inflamatoria o inmunológica (tal como la enfermedad pulmonar obstructiva crónica), diabetes, trastornos de la cognición, migrañas, epilepsia, hipertensión, o tratar afecciones asociadas con la I_{Kur} o controlar la frecuencia cardíaca.

También se proporcionan composiciones farmacéuticas que comprenden una cantidad terapéuticamente eficaz de al menos un compuesto descrito en la presente memoria descriptiva y un vehículo o transportador farmacéuticamente aceptable del mismo. Dichas composiciones pueden comprender, además, uno o más agente(s) adicionales. Por ejemplo, al menos otro agente antiarrítmico (tal como sotalol, dofetilida, diltiazem o verapamilo), o al menos un bloqueante de los canales de calcio, o al menos un agente antiplaquetario (tal como clopidogrel, cangrelor, ticlopidina, CS-747, ifetroban y aspirina), al menos un agente antihipertensor (tal como un bloqueante beta adrenérgico, inhibidor de la ECA (*p. ej.*, captopril, zofenopril, fosinopril, enalapril, ceranopril, cilazopril, delapril, pentopril, quinapril, ramipril o lisinopril), antagonista de la A II, antagonista de ET, antagonista doble de ET/AII, o inhibidor de la vasopepsidasa (*p. ej.*, omapatrilat or gemopatrilat)), o al menos un agente antitrombótico/antitrombolítico (tal como tPA, tPA recombinante, TNK, nPA, inhibidores del factor VIIa, inhibidores del factor Xa (tal como razaxaban), inhibidores del factor XIa o inhibidores de la trombina), o al menos un anticoagulante (tal como warfarina o una heparina), o al menos un inhibidor de la HMG-CoA reductasa (pravastatina, lovastatina, atorvastatina, simvastatina, NK-104 o ZD-4522), o al menos un agente antidiabético (tal

como biguanida o una combinación biguanidas/gliburida), o al menos un mimético tiroideo, o al menos un antagonista de los receptores mineralocorticoides (tal como espironolactona o eplerinona) o al menos un glicósido cardíaco (tal como digitálicos o ouabaína).

DEFINICIONES

Los términos "alc" o "alquilo" se refieren a grupos hidrocarburo de cadena lineal o ramificada que tienen de 1 a 12 átomos de carbono o de 1 a 8 átomos de carbono, tales como metilo, etilo, n-propilo, i-propilo, n-butilo, i-butilo, *t*-butilo, pentilo, hexilo, heptilo, octilo o cualquier subconjunto de los anteriores. La expresión "alquilo sustituido" se refiere a grupos alquilo sustituidos con uno o más grupos (tal como por grupos descritos en lo que antecede en la definición de R^{10}), tal como los seleccionados de arilo, arilo sustituido, heterociclo, heterociclo sustituido, carbociclo, carbociclo sustituido, halo, hidroxi, alcoxi (opcionalmente sustituido), ariloxi (opcionalmente sustituido), alquiléster (opcionalmente sustituido), ariléster (opcionalmente sustituido), alcanoílo (opcionalmente sustituido), ariol (opcionalmente sustituido), ciano, nitro, amino, amino sustituido, amido, lactama, urea, uretano y sulfonilo, o cualquier subconjunto de los anteriores.

El término "alquenilo" se refiere a grupos hidrocarburo de cadena lineal o ramificada que tienen de 2 a 12 átomos de carbono o de 2 a 4 átomos de carbono y al menos un doble enlace carbono-carbono (bien cis o bien trans), tal como etenilo. La expresión "alquenilo sustituido" se refiere a grupos alquenilo sustituidos con uno o más grupos (tal como por grupos descritos en lo que antecede en la definición de R^{10}), tal como los seleccionados de arilo,

arilo sustituido, heterociclo, heterociclo sustituido, carbociclo, carbociclo sustituido, halo, hidroxi, alcoxi (opcionalmente sustituido), ariloxi (opcionalmente sustituido), alquiléster (opcionalmente sustituido), ariléster (opcionalmente sustituido), alcanoílo (opcionalmente sustituido), ariol (opcionalmente sustituido), ciano, nitro, amino, amino sustituido, amido, lactama, urea, uretano y sulfonilo, o cualquier subconjunto de los anteriores.

El término "alquinilo" se refiere a grupos hidrocarburo de cadena lineal o ramificada que tienen de 2 a 12 átomos de carbono o de 2 a 4 átomos de carbono y al menos un triple enlace carbono-carbono (bien cis o bien trans), tal como etinilo. La expresión "alquinilo sustituido" se refiere a grupos alquinilo sustituidos con uno o más grupos (tal como por grupos descritos en lo que antecede en la definición de R^{10}), tal como los seleccionados de arilo, arilo sustituido, heterociclo, heterociclo sustituido, carbociclo, carbociclo sustituido, halo, hidroxi, alcoxi (opcionalmente sustituido), ariloxi (opcionalmente sustituido), alquiléster (opcionalmente sustituido), ariléster (opcionalmente sustituido), alcanoílo (opcionalmente sustituido), ariol (opcionalmente sustituido), ciano, nitro, amino, amino sustituido, amido, lactama, urea, uretano y sulfonilo, o cualquier subconjunto de los anteriores.

El término "arilo" se refiere a grupos aromáticos homocíclicos (es decir, hidrocarburo) que contienen anillos mono, bi o tricíclicos, tales como los que tienen de 6 a 12 miembros, tales como fenilo, naftilo y bifenilo. Fenilo es un ejemplo de un grupo arilo. La expresión "arilo sustituido" se refiere a grupos arilo sustituidos con uno o más grupos (tal como por grupos descritos en lo que antecede en la definición de R10), tal como los seleccionados de alquilo, alquilo sustituido, alquenilo (opcionalmente sustituido), arilo (opcionalmente

sustituido), heterociclo (opcionalmente sustituido), halo, hidroxi, alcoxi (opcionalmente sustituido), ariloxi (opcionalmente sustituido), alcanoílo (opcionalmente sustituido), aroílo (opcionalmente sustituido), alquiléster (opcionalmente sustituido), ariléster (opcionalmente sustituido), ciano, nitro, amino, amino sustituido, amido, lactama, urea, uretano y sulfonilo, o cualquier subconjunto de los anteriores, cuando opcionalmente uno o más pares de sustituyentes junto con los átomos a los que están unidos forman un anillo de 3 a 7 miembros.

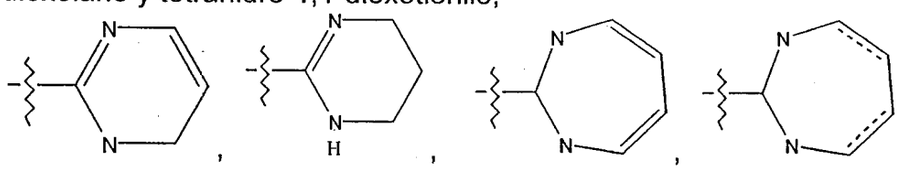
El término "cicloalquilo" se refiere a grupos de anillo mono, bi o trihomocíclicos de 3 a 15 átomos de carbono que están, respectivamente, completamente saturados y parcialmente insaturados. Los anillos de los grupos cicloalquilo multi-anillo pueden estar condensados, formando puentes y/o unidos a través de una o más uniones espiro. La expresión "cicloalquilo sustituido" se refiere a un grupo cicloalquilo sustituido con uno o más grupos (tal como por grupos descritos en lo que antecede en la definición de R^{10}), tal como los seleccionados de arilo, arilo sustituido, heterociclo, heterociclo sustituido, carbociclo, carbociclo sustituido, halo, hidroxi, alcoxi (opcionalmente sustituido), ariloxi (opcionalmente sustituido), alquiléster (opcionalmente sustituido), ariléster (opcionalmente sustituido), alcanoílo (opcionalmente sustituido), ariol (opcionalmente sustituido), ciano, nitro, amino, amino sustituido, amido, lactama, urea, uretano y sulfonilo, o cualquier subconjunto de los anteriores.

Los términos "halógeno" y "halo" se refieren a flúor, cloro, bromo y yodo.

Los términos "heterociclo", "heterocíclico", "grupo heterocíclico" o "heterociclo" se refieren a grupos cíclicos totalmente saturados o parcial o

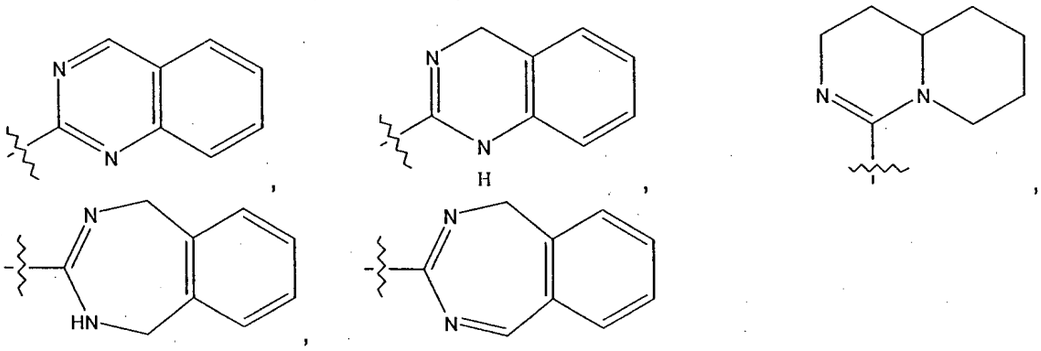
completamente insaturados, incluidos grupos aromáticos ("heteroarilo") o no aromáticos (por ejemplo, sistemas de anillos monocíclicos de 3 a 13 miembros, bicíclicos de 7 a 17 miembros o tricíclicos de 10 a 20 miembros, tales como, en ciertas formas de realización un anillo monocíclico o bicíclico que contiene un total de 3 a 10 átomos de anillo), que tienen al menos un heteroátomo en al menos un anillo que contiene un átomo de carbono. Cada anillo del grupo heterocíclico que contiene un heteroátomo puede tener 1, 2, 3 ó 4 heteroátomos seleccionados de átomos de nitrógeno, átomos de oxígeno y/o átomos de azufre, en los que los heteroátomos de nitrógeno y de azufre pueden estar oxidados, opcionalmente, y los heteroátomos pueden estar opcionalmente cuaternizados. El grupo heterocíclico puede estar unido en cualquier heteroátomo o átomo de carbono del anillo o sistema de anillos. Los anillos de los heterociclos multi-anillo pueden estar condensados, formando puentes y/o unidos a través de una o más uniones espiro.

Ejemplos de grupos heterocíclicos monocíclicos incluyen azetidinilo, pirrolidinilo, pirrolilo, pirazolilo, oxetanilo, pirazolinilo, imidazolilo, imidazolinilo, imidazolidinilo, oxazolilo, oxazolidinilo, isoxazolinilo, isoxazolilo, tiazolilo, tiadiazolilo, tiazolidinilo, isotiazolilo, isotiazolidinilo, furilo, tetrahidrofurilo, tienilo, oxadiazolilo, piperidinilo, piperazinilo, 2-oxopiperazinilo, 2-oxopiperidinilo, 2-oxopirrolidinilo, 2-oxazepinilo, azepinilo, 4 piperidonilo, piridilo, pirazinilo, pirimidinilo, piridazinilo, triazinilo, tetrahidropiranilo, tetrazolio, triazolilo, morfolinilo, tiomorfolinilo, tiomorfolinilo sulfóxido, tiomorfolinilo sulfona, 1,3-dioxolano y tetrahidro-1,1-dioxotienilo,



y similares.

Entre los ejemplos de grupos heterocíclicos bicíclicos se incluyen indolilo, benzotiazolilo, benzoxazolilo, benzotienilo, quinuclidinilo, quinolinilo, tetra-hidroisoquinolinilo, isoquinolinilo, bencimidazolilo, benzopiranilo, indolizinilo, benzofurilo, benzofuranilo, dihidrobenzofuranilo, cromonilo, coumarinilo, benzodioxolilo, dihidrobenzodioxolilo, benzodioxinilo, cinnolinilo, quinoxalinilo, indazolilo, pirrolopiridilo, furopiridinilo (tal como furo[2,3-c]piridinilo, furo[3,2-b]piridinilo] o furo[2,3-b]piridinilo), dihidroisoindolilo, dihidroquinazolinilo (tal como 3,4-dihidro-4-oxo-quinazolinilo), tetrahidroquinolinilo, azabicicloalquilos (tal como 6-azabiciclo[3.2.1]octano), azaespiroalquilos (tal como 1,4 dioxa-8-azaespiro[4.5]decano), imidazopiridinilo (tal como imidazo[1,5-a]piridin-3-ilo), triazolopiridinilo (tal como 1,2,4-triazolo[4,3-a]piridin-3-ilo), y hexahidroimidazopiridinilo (tal como 1,5,6,7,8,8a-hexahidroimidazo[1,5-a]piridin-3-ilo),



y similares.

Entre los ejemplos de grupos heterocíclicos tricíclicos se incluyen carbazolilo bencidolilo, fenantrolinilo, acridinilo, fenantridinilo, xantenilo y similares.

Las expresiones “heterociclo sustituido”, “heterocíclico sustituido”, “grupo

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heterocíclico sustituido" y "heterociclo sustituido" se refieren a grupos heterociclo, heterocíclicos y heterociclos sustituidos con uno o más grupos (tal como por grupos descritos en lo que antecede en la definición de R^{10}), tal como los seleccionados de alquilo, alquilo sustituido, alquenilo, oxo, arilo, arilo sustituido, heterociclo, heterociclo sustituido, carbociclo (opcionalmente sustituido), halo, hidroxi, alcoxi (opcionalmente sustituido), ariloxi (opcionalmente sustituido), alcanoílo (opcionalmente sustituido), aroílo (opcionalmente sustituido), alquiléster (opcionalmente sustituido), ariléster (opcionalmente sustituido), ciano, nitro, amido, amino, amino sustituido, lactama, urea, uretano, sulfonilo, o cualquier subconjunto de los anteriores, cuando opcionalmente uno o más pares de sustituyentes junto con los átomos a los que están unidos forman un anillo de 3 a 7 miembros.

El término "alcanoílo" se refiere a grupo alquilo (que puede estar opcionalmente sustituid como se ha descrito en lo que antecede) unido a un grupo carbonilo (*es decir*, -C(O)-alquilo). De forma similar, el término "aroílo" se refiere a cualquier grupo arilo (que puede estar opcionalmente sustituid como se ha descrito en lo que antecede) unido a un grupo carbonilo (*es decir*, -C(O)-arilo).

A lo largo de la memoria descriptiva se pueden escoger grupos y sustituyentes de los mismos proporcionando restos estables y compuestos.

Los compuestos descritos en la presente memoria descriptiva forman sales o solvatos, que también están dentro del alcance de la presente invención. La referencia a un compuesto descrito en la presente memoria descriptiva se entiende que incluye referencia a sus sales, a menos que se indique lo contrario. El término "sal(es)", como se emplea en la presente

memoria descriptiva, indica sales ácidas y/o básicas formadas con ácidos y bases orgánicos y/o inorgánicos. Además, cuando un compuesto descrito en la presente memoria descriptiva contiene un resto básico y un resto ácido se pueden formar zwiteriones ("sales internas" y están incluidas dentro del término "sal(es)" tal como se usa en la presente memoria descriptiva. Se prefieren las sales farmacéuticamente aceptables (*es decir*, no tóxicas, fisiológicamente aceptables), aunque también son útiles otras sales en, *por ejemplo*, etapas de aislamiento o purificación que pueden emplearse durante la preparación. Se pueden formar sales de los compuestos descritos en la presente memoria descriptiva mediante, por ejemplo, reacción de un compuesto con una cantidad de ácido o base, tal como una cantidad equivalente, en un medio tal como uno en el que la sal precipita o en un medio acuoso seguido por liofilización.

Los compuestos descritos en la presente memoria descriptiva que contienen un resto básico pueden formar sales con diversos ácidos orgánicos e inorgánicos. Ejemplos de sales de adición de ácido incluyen acetatos (tal como las formadas con ácido acético o ácido trihaloacético, por ejemplo ácido trifluoroacético), adipatos, alginatos, ascorbatos, aspartatos, benzoatos, bencenosulfonatos, bisulfatos, boratos, butiratos, citratos, alcanforatos, alcanforsulfonatos, ciclopentanopropionatos, digluconatos, dodecilsulfatos, etanosulfonatos, fumaratos, glucoheptanoatos, glicerofosfatos, hemisulfatos, heptanoatos, hexanoatos, clorhidratos (formados con ácido clorhídrico), bromhidratos (formados con bromuro de hidrógeno), yodhidratos, 2-hidroxietanesulfonatos, lactatos, maleatos (formados con ácido maleico), metanosulfonatos (formados con ácido metanosulfónico), 2-naftalenosulfonatos, nicotinatos, nitratos, oxalatos, pectinatos, persulfatos, 3-

fenilpropionatos, fosfatos, picratos, pivalatos, propionatos, salicilatos, succinatos, sulfatos (tales como los formados con ácido sulfúrico), sulfonatos (tales como los mencionados en la presente memoria descriptiva), tartratos, tiocianatos, toluenosulfonatos tales como tosilatos, undecanoatos, y similares.

Los compuestos descritos en la presente memoria descriptiva que contienen un resto ácido pueden formar sales con diversos bases orgánicas e inorgánicas. Ejemplo de sales básicas incluyen sales de amonio, sales de metales alcalinos tales como sales de sodio, litio y potasio, sales de metales alcalino-térreos tales como sales de calcio y de magnesio, sales con bases orgánicas (por ejemplo aminas orgánicas), tales como benzatinas, diciclohexilaminas, hidrabaminas (formadas con N,N-bis(dehidroabietil)etilendiamina), N-metil-D-glucaminas, N-metil-D-glucamidas, *t*-butilaminas, y sales con aminoácidos tales como arginina y lisina, y similares.

Los grupos que contienen nitrógeno básico pueden cuaternizarse con agentes tales como haluros de alquilo inferior (*p. ej.*, cloruros, bromuros y yoduros de metilo, etilo, propilo y butilo), sulfatos de dialquilo (*p. ej.*, sulfatos de dimetilo, dietilo, dibutilo y diamilo), haluros de cadena larga (*p. ej.*, cloruros, bromuros y yoduros de decilo, laurilo, miristilo y estearilo), haluros de aralquilo (*p. ej.*, bromuros de bencilo y fenetilo) y otros.

Cualquier compuesto que se puede convertir un vivo proporcionando el agente bioactivo (*es decir*, el compuesto de fórmula (I) es un profármaco dentro del alcance y espíritu de la invención.

El término "profármacos", como se emplea en la presente memoria descriptiva, incluye ésteres y carbonatos formados mediante la reacción de uno o más hidroxilos de los compuestos de fórmula I con agentes acilantes

sustituidos con alquilo, alcoxi o arilo, mediante procedimientos que los expertos en la técnica saben que generan acetatos, pivalatos, metilcarbonatos, benzoatos y similares.

En la técnica se conocen bien varias formas de profármacos y se describen en:

a) Wermuth, C.G. y col., *The Practice of Medicinal Chemistry*, Capítulo 31, Academic Press (1996);

b) *Design of Prodrugs*, H. Bundgaard, ed., Elsevier (1985);

c) Bundgaard, H., Capítulo 5, "Design and Application of Prodrugs," *A Textbook of Drug Design and Development*, pp. 113-191, P. Krosgaard-Larsen y col., eds., Harwood Academic Publishers (1991); y

d) Testa, B. y col., *Hydrolysis in Drug and Prodrug Metabolism*, Wiley-VCH (2003).

Además, preferentemente, los compuestos descritos en la presente memoria descriptiva , después de su preparación, se aíslan y purifican obteniendo una composición que contiene una cantidad en peso igual o superior al 99% del compuesto descrito en la presente memoria descriptiva (compuesto "sustancialmente puro"), que después se usa o formula como se ha descrito en la presente memoria descriptiva. Dichos compuestos "sustancialmente puros" descrito en la presente memoria descriptiva también se contemplan en la presente memoria descriptiva como parte de la presente invención.

En la medida que los compuestos descritos en la presente memoria descriptiva, y sus sales, pueden existir en su forma tautomérica, todas estas

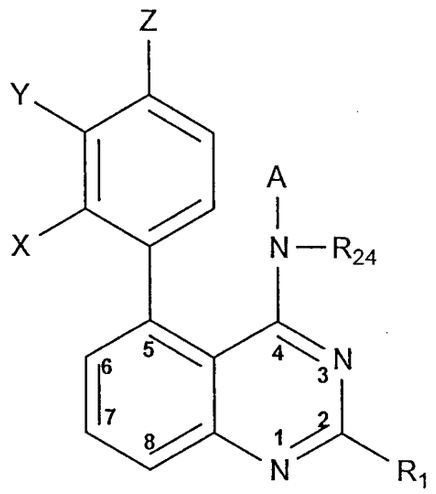
formas tautoméricas se contemplan en la presente memoria descriptiva como parte de la presente invención.

Todos los estereoisómeros de los presentes compuestos, tales como los que pueden existir incluso en ausencia de carbonos asimétricos) y formas diaestereoméricas están contempladas dentro del alcance de la presente invención. Estereoisómeros individuales de los compuestos de la invención pueden, por ejemplo, estar sustancialmente libres de otros isómeros, o pueden mezclarse como, por ejemplo, racematos o con todos los demás estereoisómeros, u otros seleccionados.

Con los términos "que incluye", "tal como", "por ejemplo" y similares se pretende hacer referencia a formas de realización de ejemplo y no limitar el alcance de la presente invención.

DESCRIPCIÓN DETALLADA DE LA INVENCIÓN

De acuerdo con la presente invención, se proporcionan compuestos de fórmula I



I

o enantiómeros, diastereómeros, tautómeros, profármacos o sales de los

mismos, en la que:

X es H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-NR_{11}SO_2R_{12}$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-NR_{11}SO_2NR_{11}R_{12}$, $-OCONR_{11}R_{12}$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Y es H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-NR_{11}SO_2R_{12}$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-NR_{11}SO_2NR_{11}R_{12}$, $-OCONR_{11}R_{12}$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Z es H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-NR_{11}SO_2R_{12}$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-NR_{11}SO_2NR_{11}R_{12}$, $-OCONR_{11}R_{12}$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

A es $-(CH_2)_m-R_2$, $-CH(R_{25})(R_{26})$, $-(CH_2)_m-C(O)-R_{2a}$, $-CH(R_{26})-CO_2-R_{2a}$ o $-(CH_2)_{n-1}-NR_{25}-CO_2-R_{24}$;

m es 0 a 4;

n es 1 a 4;

n-1 es 2 a 4;

R_1 es -OH, F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, cicloalquilo C_{3-10}, -CN, $-(CH_2)_m-SO_2R_{11}$, $-(CH_2)_n-SO_2NR_{11}R_{12}$, $-(CH_2)_n-CO_2R_{11}$ o $-(CH_2)_n-NR_{11}SO_2R_{12}$, pudiendo estar el alquenilo y cicloalquilo opcionalmente sustituidos con uno o más R_{13}; o

R_1 es un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, en el que: (i) el heteroarilo y heterociclilo están opcionalmente sustituidos con uno o más R_{13a}, R_{13b}, R_{13c}, R_{13d}, R_{13e}, R_{13f}, R_{13g}, R_{13h}, R_{13hh}, R_{13j}, R_{13m}, R_{13m-1}, R_{13n-1}, R_{13p}, R_{13p-1}, R_{13q} y R_{13q-1}; (ii) el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y (iii) el heteroarilo y heterociclilo están conectados al anillo quinazolinilo a través de un átomo de carbono; o

R_1 es fenilo, que puede estar opcionalmente sustituido con uno o más R_{13aa}, R_{13bb}, R_{13cc}, R_{13dd} y R_{13ee};

R_2 es alquilo C_{1-10}, cicloalquilo C_{3-10}, cicloalquenilo C_{3-10} o $-NR_{14}R_{14}$, en el que el cicloalquilo puede estar opcionalmente sustituido con uno o más R_{13} o R_{13bb} y el cicloalquenilo puede estar opcionalmente sustituido con uno o más R_{13b}; con la condición de que R_2 no sea $-NR_{14}R_{14}$ cuando m sea 0, 1 ó 3; o

R_2 es arilo C_{6-10}, que está opcionalmente sustituido con uno o más R_{13a-1}, R_{13b-1}, R_{13c-1}, R_{13d-1} y R_{13e-1}; o

R_2 es un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, los cuales están ambos opcionalmente sustituidos con uno o más R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d-2}, R_{13e-2}, R_{13g-2}, R_{13a-4}, R_{13b-4}, R_{13c-4}, R_{13d-4}, R_{13b-5}, R_{13c-5}, R_{13h-1}, R_{13hh-1}, R_{13hh-2}, R_{13m-1}, R_{13n-1}, R_{13n-2}, R_{13p-1}, R_{13p-2}, R_{13q-1} y R_{13q-2}s; y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{2a} es alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, $-NR_{14}R_{14}$, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, cualquiera de los

cuales está opcionalmente sustituido con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{11} y R_{12}, en cada aparición, se seleccionan independientemente de H, alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros y un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

R_{11} y R_{12} se toman junto con el nitrógeno al que están unidos formando un heterociclilo de 4 a 12 miembros, pudiendo estar el heterociclilo opcionalmente sustituido con uno o más R_{13} y el heterociclilo está constituido por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo,

alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; con la condición de que cuando R_{13} sea alquilo sustituido con un R_{14a}, R_{14a} no sea -OH;

R_{13a}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13aa}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, -

000524

$NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, -

$NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-$

$NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13bb}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, -

$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de

4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12},

alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_n-OCONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13cc}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$, o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I,

alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo

constituido por N, S u O;

R_{13d}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13dd}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y

1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más

R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo,

alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13ee}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, -

$CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13f}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, -

$NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, -

$NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13h}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13h-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-$

$NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, -

$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13j}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de

4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13m}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13m-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12},

alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13n-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13p}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I,

alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13p-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13p-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo

constituido por N, S u O;

R_{13q-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y

1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{14} se toman junto con los átomos a los que están unidos formando un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-NO_2$, $-CO_2H$, $-CO_2R_{26}$, $-OCONR_{24}R_{24}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, =O, $-CONR_{24}R_{24}$, $-COR_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$, $-NR_{24}CO_2R_{24}$, $-SO_2NR_{24}R_{24}$, o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y

heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{24} se toman junto con los átomos a los que están unidos formando un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, =O, $-CONR_{25}R_{25}$, $-COR_{25}$, $-NR_{25}R_{25}$, $-NR_{25}CO_2R_{25}$, o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O.

En una realización, se proporcionan compuestos, enantiómeros,

diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que R_1 es un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, en el que: (i) el heteroarilo y heterociclilo están opcionalmente sustituidos con uno o más R_{13a}, R_{13b}, R_{13c}, R_{13d}, R_{13e}, R_{13f}, R_{13g}, R_{13h}, R_{13hh}, R_{13j}, R_{13m}, R_{13m-1}, R_{13n-1}, R_{13p}, R_{13p-1}, R_{13q} y R_{13q-1}; (ii) el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y (iii) el heteroarilo y heterociclilo están conectados al anillo quinazolinilo a través de un átomo de carbono.

En otras realizaciones de la invención, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que R_1 es -OH, F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, cicloalquilo C_{3-10}, -CN, $-(CH_2)_m-SO_2R_{11}$, $-(CH_2)_n-SO_2NR_{11}R_{12}$, $-(CH_2)_n-CO_2R_{11}$ o $-(CH_2)_n-NR_{11}SO_2R_{12}$, pudiendo estar el alquenilo y cicloalquilo opcionalmente sustituidos con uno o más R_{13}.

En otra realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que R_2 es arilo C_{6-10}, que está opcionalmente sustituido con uno o más R_{13a-1}, R_{13b-1}, R_{13c-1}, R_{13d-1} y R_{13e-1}.

En otra realización más, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que R_2 es un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, los cuales están ambos opcionalmente sustituidos con uno o más R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d-2}, R_{13e-2}, R_{13g-2}, R_{13a-4}, R_{13b-4}, R_{13c-4}, R_{13d-4}, $R13_{b-5}$, R_{13c-5}, R_{13h-1}, R_{13hh-1}, R_{13hh-2}, R_{13m-1}, R_{13n-1}, R_{13n-2}, $R13_{p-1}$, R_{13p-2}, R_{13q-1} y R_{13q-2}; y el

heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O.

En una realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que R_2 es un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, los cuales están ambos opcionalmente sustituidos con uno o más R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d-2}, R_{13e-2}, R_{13g-2}, R_{13a-4}, R_{13b-4}, R_{13c-4}, R_{13d-4}, $R13_{b-5}$, R_{13c-5}, R_{13h-1}, R_{13hh-1}, R_{13hh-2}, R_{13m-1}, R_{13n-1}, R_{13n-2}, $R13_{p-1}$, R_{13p-2}, R_{13q-1} y R_{13q-2}; y el heteroarilo y heterociclilo están constituidos por átomos de carbono y al menos un heteroátomo N.

En otra realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que:

X es H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-NR_{11}SO_2R_{12}$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-NR_{11}SO_2NR_{11}R_{12}$, $-OCONR_{11}R_{12}$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Y es H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-NR_{11}SO_2R_{12}$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-NR_{11}SO_2NR_{11}R_{12}$, $-OCONR_{11}R_{12}$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Z es H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10},

alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 6 a 12 miembros, heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-NR_{11}SO_2R_{12}$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-NR_{11}SO_2NR_{11}R_{12}$, $-OCONR_{11}R_{12}$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

A es $-(CH_2)_m-R_2$, $-CH(R_{25})(R_{26})$, $-(CH_2)_m-C(O)-R_{2a}$, $-CH(R_{26})-CO_2-R_{2a}$ o $-(CH_2)_{n-1}-NR_{25}-CO_2-R_{24}$;

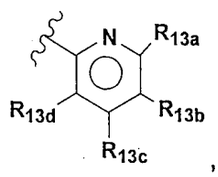
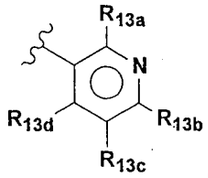
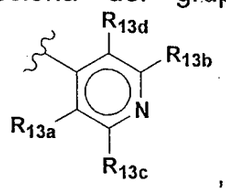
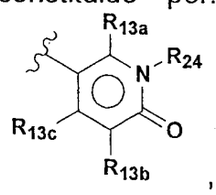
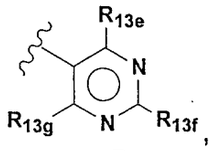
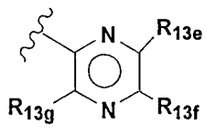
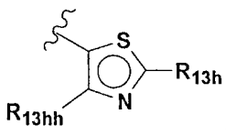
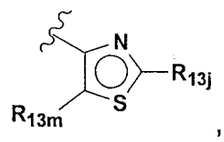
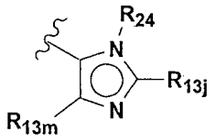
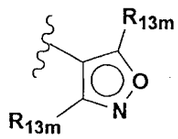
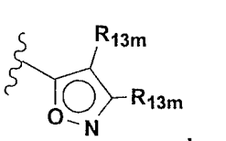
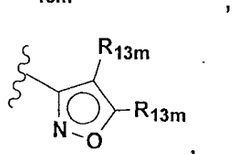
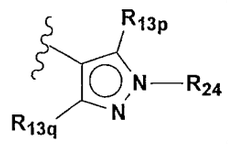
m es 0 a 4;

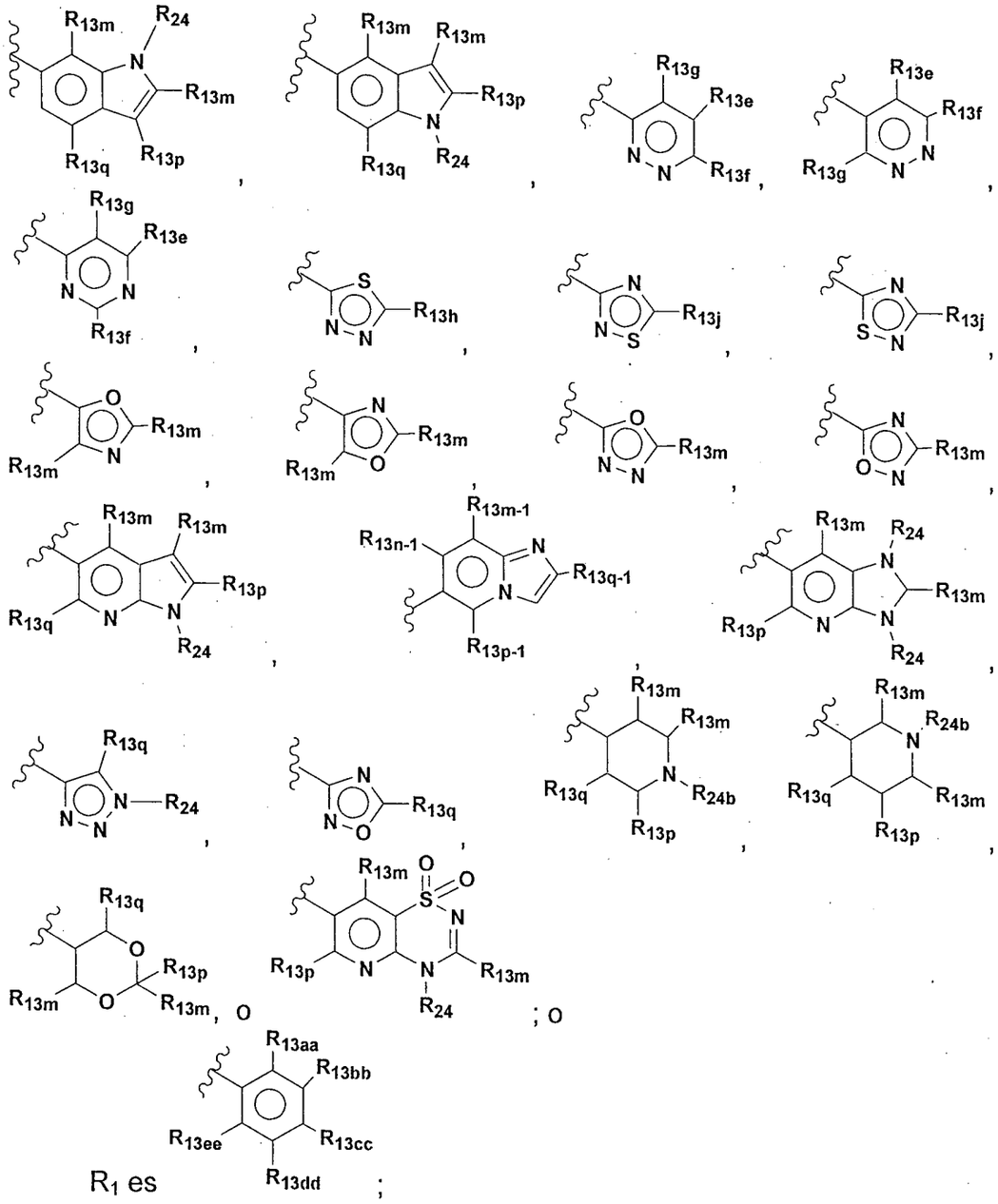
n es 1 a 4;

n-1 es 2 a 4;

R_1 es -OH, F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, cicloalquilo C_{3-10}, -CN, $-(CH_2)_m-SO_2R_{11}$, $-(CH_2)_n-SO_2NR_{11}R_{12}$, $-(CH_2)_n-CO_2R_{11}$ o $-(CH_2)_n-NR_{11}SO_2R_{12}$, pudiendo estar el alquenilo y cicloalquilo opcionalmente sustituidos con uno o más R_{13}; o

R_1 se selecciona del grupo constituido por:

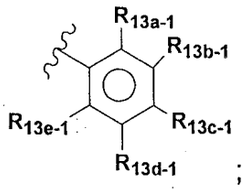
















R_1 es

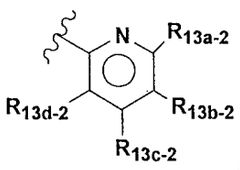
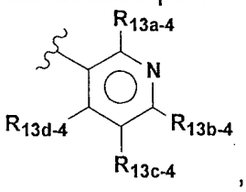
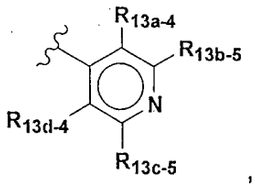
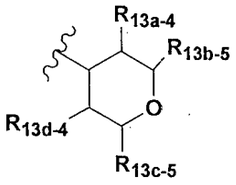
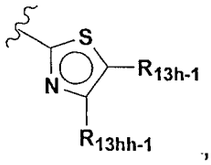
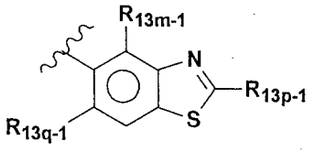
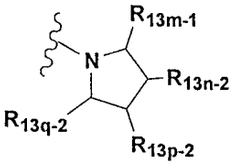
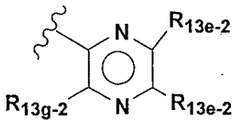
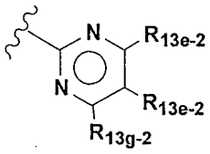
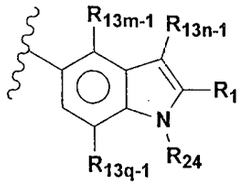
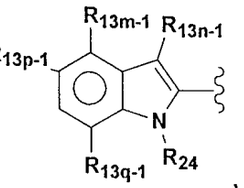
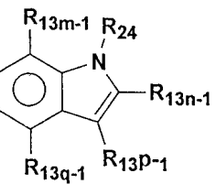
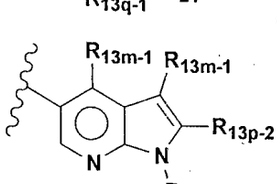
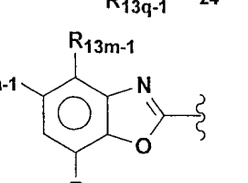
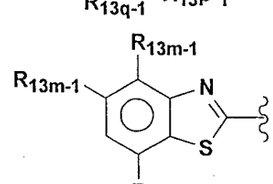
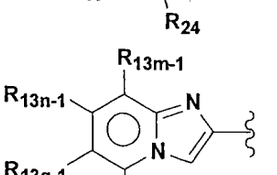
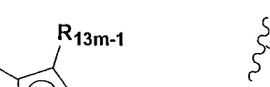
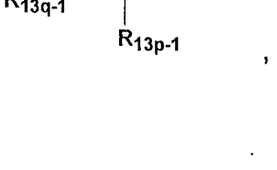
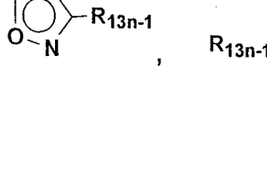
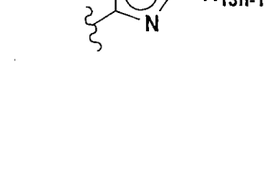
;

R_2 es alquilo C_{1-10}, ciclopropilo opcionalmente sustituido con uno o más R_{13}; cicloalquilo C_{4-10} opcionalmente sustituido con uno o más R_{13bb}; cicloalquenilo C_{3-10} opcionalmente sustituido con uno o más R_{13b}; o $-NR_{14}R_{14}$; con la condición de que R_2 no sea $-NR_{14}R_{14}$ cuando m sea 0, 1 ó 3; o



R_2 es ; o

R_2 se selecciona del grupo constituido por:

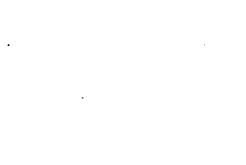

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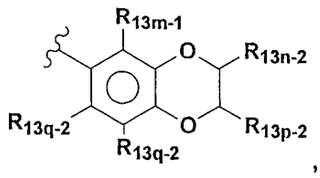
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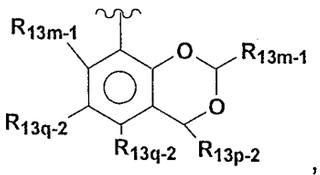
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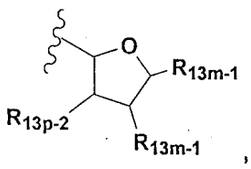
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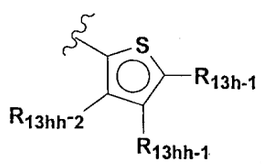
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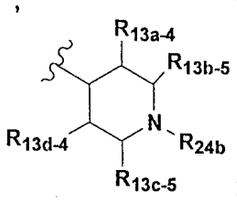
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;

R_{2a} es alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, $-NR_{14}R_{14}$, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, cualquiera de los cuales está opcionalmente sustituido con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{11} y R_{12}, en cada aparición, se seleccionan independientemente de H, alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros y un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

R_{11} y R_{12} se toman junto con el nitrógeno al que están unidos formando un heterociclilo de 4 a 12 miembros, pudiendo estar el heterociclilo opcionalmente sustituido con uno o más R_{13} y el heterociclilo está constituido por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I,

alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; con la condición de que cuando R_{13} sea alquilo sustituido con un R_{14a}, R_{14a} no sea -OH;

R_{13a}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo

constituido por N, S u O;

R_{13aa}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y

1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más

R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13bb}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo,

alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, -

$CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, -

$NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-(CH_2)_n-OCONR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13cc}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, -

$NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$, o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 6 a 12 miembros, un heterociclilo de 6 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-$

$NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, -

$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13dd}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de

4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12},

alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I,

alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13ee}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo

constituido por N, S u O;

R_{13f}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y

1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13h}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más

R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13h-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{7-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo,

alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, -

$CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13j}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13m}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, -

$NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13m-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13n-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, -

$NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13p}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13p-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-$

$NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13p-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, -

$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de

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4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{14} se toman junto con los átomos a los que están unidos formando un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-NO_2$, $-CO_2H$, $-CO_2R_{26}$, $-OCONR_{24}R_{24}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, =O, $-CONR_{24}R_{24}$, -

COR_{24}, $-SO_2R_{24}$, $-NR_{24}R_{24}$, $-NR_{24}CO_2R_{24}$, $-SO_2NR_{24}R_{24}$, o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{24} se toman junto con los átomos a los que están unidos formando un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, =O, $-CONR_{25}R_{25}$, $-COR_{25}$, $-NR_{25}R_{25}$, $-NR_{25}CO_2R_{25}$, o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24b}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, $-CO_2R_{25}$, $-SO_2NR_{25}R_{25}$, $-COR_{25}$ o aril C_{6-10}-

alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

con la condición de que:

(i) R_1 no sea Cl cuando m sea 0, 1 ó 2; R_{13a-1} sea H, $-CF_3$, o metoxi; R_{13c-1} sea H, OH, metoxi o dimetilamino; X, Y, Z, R_{13b-1}, R_{13d-1}, R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d-2}, R_{13e-2}, R_{13g-2}, R_{13a-4}, R_{13b-4}, R_{13c-4}, R_{13d-4}, R_{13b-5}, R_{13c-5}, R_{13m-1}, R_{13n-1}, R_{13p-1} y R_{13q-1} sean H; y

(ii) m no sea 0 ó 1 cuando X, Y, R_{13a}, R_{13d}, R_{13e}, R_{13g}, R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d-2}, R_{13a-4}, R_{13b-4}, R_{13c-4}, R_{13d-4} R_{13b-5}, R_{13c-5}, R_{13h-1} y R_{13hh-1} sean H; R_{13b} sea H o $-SO_2NH_2$; R_{13c} sea H, $-CONH_2$, $-SO_2N(C_2H_4OH)_2$, $-SO_2NHCOCH_3$, $-SO_2NH_2$, -tetrazolilo o (4-aminopiperidinil)sulfonilo; R_{13f} sea H o $-NHC_2H_4OCH_3$; y Z sea H, $-CO_2H$, o $-CO_2CH_3$.

En otra realización más, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I,

en la que:

X es H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-NR_{11}SO_2R_{12}$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-NR_{11}SO_2NR_{11}R_{12}$, $-OCONR_{11}R_{12}$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Y es H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alqueniló C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-NR_{11}SO_2NR_{11}R_{12}$, $-OCONR_{11}R_{12}$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Z es H, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 6 a 12 miembros, heterociclilo de 4 a 12 miembros, $-NO_2$, $-NR_{11}SO_2R_{12}$, $-SO_2NR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-NR_{11}SO_2NR_{11}R_{12}$, $-OCONR_{11}R_{12}$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

A es $-(CH_2)_m-R_2$, $-CH(R_{25})(R_{26})$, $-CH(R_{26})-CO_2-R_{2a}$ o $-(CH_2)_{n-1}-NR_{25}-CO_2-R_{24}$;

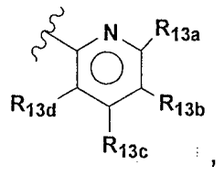
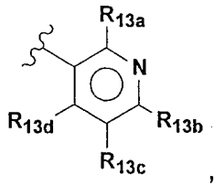
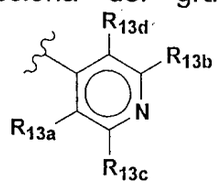
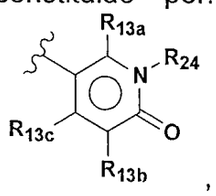
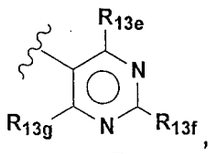
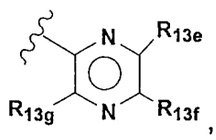
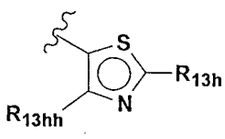
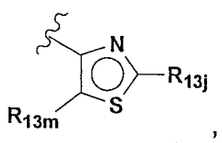
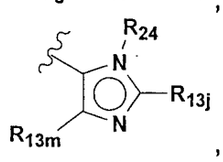
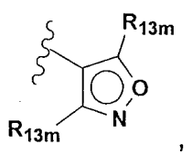
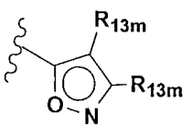
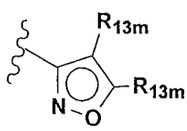
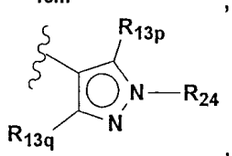
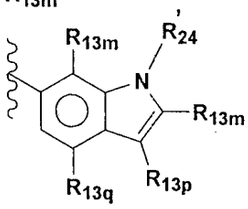
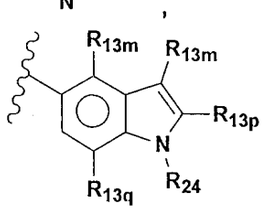
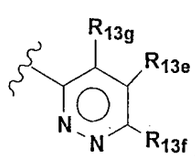
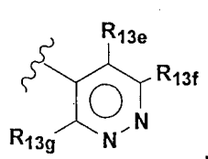
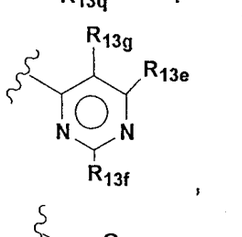
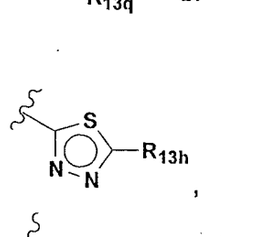
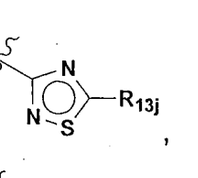
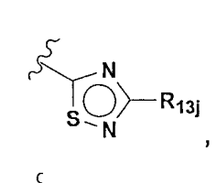
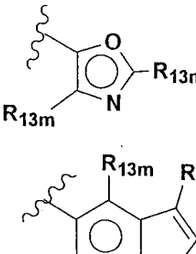
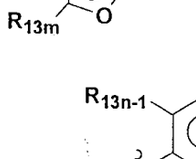
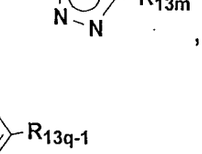
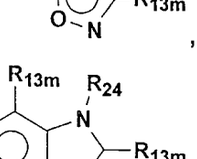
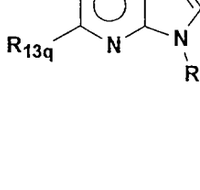
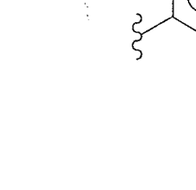
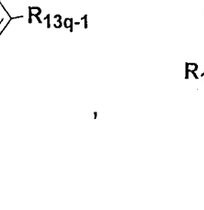
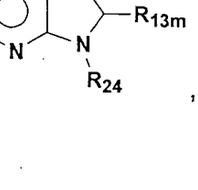
m es 0 a 4;

n es 1 a 4;

n-1 es 2 a 4;

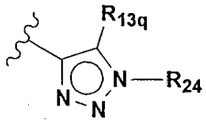
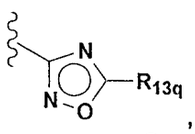
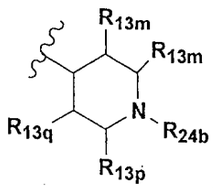
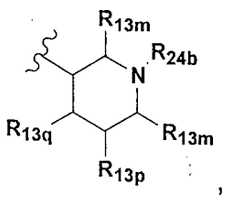
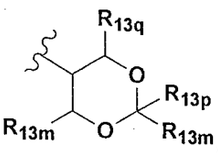
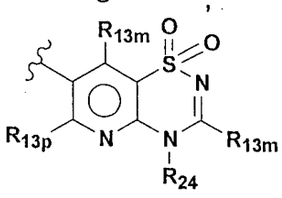
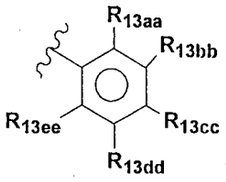
R_1 es -OH, F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, cicloalquilo C_{3-10}, -CN, $-(CH_2)_n-SO_2NR_{11}R_{12}$, $-(CH_2)_n-CO_2R_{11}$ o $-(CH_2)_n-NR_{11}SO_2R_{12}$, pudiendo estar el alquenilo y cicloalquilo opcionalmente sustituidos con uno o más R_{13}; o

R_1 se selecciona del grupo constituido por:

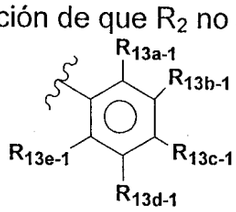



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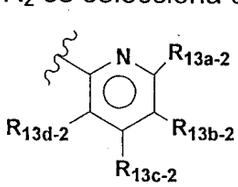
R_1 es ;

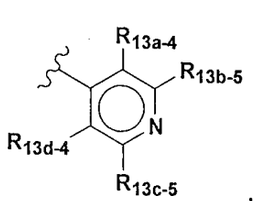
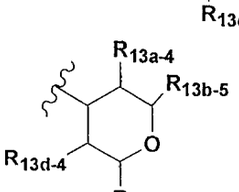
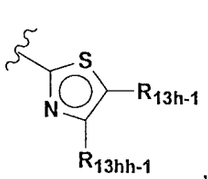
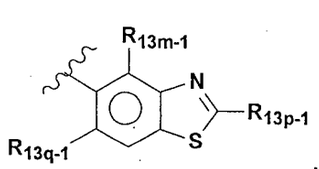
R_2 es alquilo C_{1-10}, ciclopropilo opcionalmente sustituido con uno o más R_{13}; cicloalquilo C_{4-10} opcionalmente sustituido con uno o más R_{13bb}; cicloalquenilo C_{3-10} opcionalmente sustituido con uno o más R_{13b}; o $-NR_{14}R_{14}$; con la condición de que R_2 no sea $-NR_{14}R_{14}$ cuando m sea 0, 1 ó 3; o

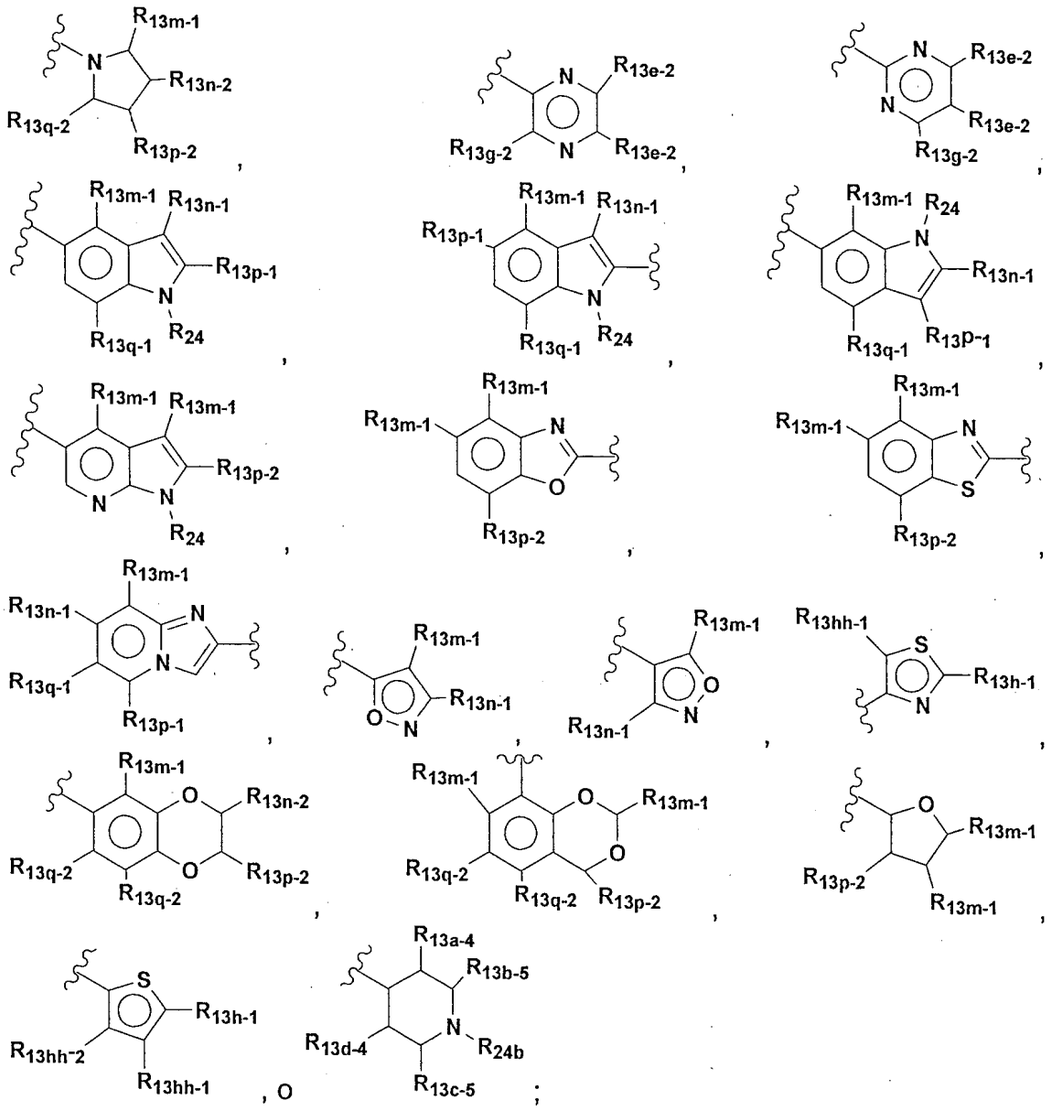


R_2 es ; o

R_2 se selecciona del grupo constituido por:





R_{2a} es alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, $-NR_{14}R_{14}$, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, cualquiera de los cuales está opcionalmente sustituido con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{11} y R_{12}, en cada aparición, se seleccionan independientemente de H,

alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros y un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

R_{11} y R_{12} se toman junto con el nitrógeno al que están unidos formando un heterociclilo de 4 a 12 miembros, pudiendo estar el heterociclilo opcionalmente sustituido con uno o más R_{13} y el heterociclilo está constituido por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; con la condición de que cuando R_{13} sea alquilo sustituido con un R_{14a}, R_{14a} no sea -OH;

R_{13a}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13aa}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo

constituido por N, S u O;

R_{13a-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2}, en cada aparición, es independientemente H, -OH, F, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y

1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y

heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13bb}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo,

heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo

estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-(CH_2)_n-OCONR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo

estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13cc}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$, o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 6 a 12 miembros, un heterociclilo de 6 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, $-NO_2$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-NR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo

opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-4}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo,

alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, -

$CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13dd}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, -

$NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, -

$NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13ee}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, -

$NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-1}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, -

$NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13f}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-$

$NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13h}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, -

$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13h-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{7-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de

4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12},

alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13j}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13m}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I,

alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13m-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13n-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13p}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo

constituido por N, S u O;

R_{13p-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13p-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y

1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más

R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{14} se toman junto con los átomos a los que están unidos formando un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con

uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-NO_2$, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, =O, $-CONR_{24}R_{24}$, $-COR_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$, $-NR_{24}CO_2R_{24}$, $-SO_2NR_{24}R_{24}$, o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{24} se toman junto con los átomos a los que están unidos formando un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, =O, $-CONR_{25}R_{25}$, $-COR_{25}$, $-NR_{25}R_{25}$, $-NR_{25}CO_2R_{25}$, o aril C_{6-10}-

alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24b}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, $-CO_2R_{25}$, $-SO_2NR_{25}R_{25}$, $-COR_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

con la condición de que:

(i) R_1 no sea Cl cuando m sea 0, 1 ó 2; R_{13a-1} es H, $-CF_3$, o metoxi; R_{13c-1} es H, OH, metoxi o dimetilamino; X, Y, Z, R_{13b-1}, R_{13d-1}, R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d-2}, R_{13e-2}, R_{13g-2}, R_{13a-4}, R_{13b-4}, R_{13c-4}, R_{13d-4}, R_{13b-5}, R_{13c-5}, R_{13m-1}, R_{13n-1}, R_{13p-1} y R_{13q-1} son H; y

(ii) m no sea 0 ó 1 cuando X, Y, R_{13a}, R_{13d}, R_{13e}, R_{13g}, R_{13a-2}, R_{13b-2}, R_{13c-}

$_{2}$, R_{13d-2}, R_{13a-4}, R_{13b-4}, R_{13c-4}, R_{13d-4} R_{13b-5}, R_{13c-5}, R_{13h-1} y R_{13hh-1} sean H; R_{13b} sea H o $-SO_2NH_2$; R_{13c} sea H, $-CONH_2$, $-SO_2N(C_2H_4OH)_2$, $-SO_2NHCOCH_3$, $-SO_2NH_2$, -tetrazolilo o (4-aminopiperidinil)sulfonilo; R_{13f} sea H o $-NHC_2H_4OCH_3$; y Z es H, $-CO_2H$, o $-CO_2CH_3$.

En una realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que X es H.

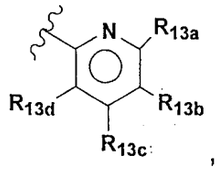
En otra realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que X e Y son H.

En otra realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que X, Y y Z son H.

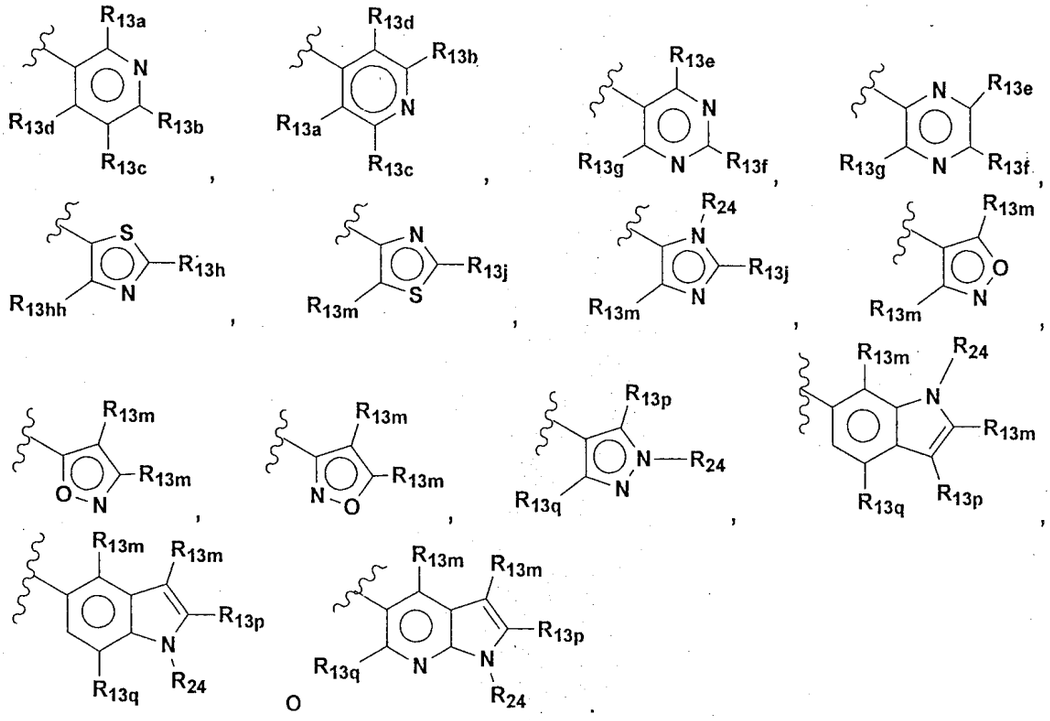
En una realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que R_1 es F, Cl, Br o I.

En una realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que R_1 es Cl.

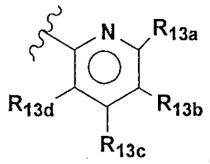
En una realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I,

en la que R_1 se selecciona del grupo constituido por: 

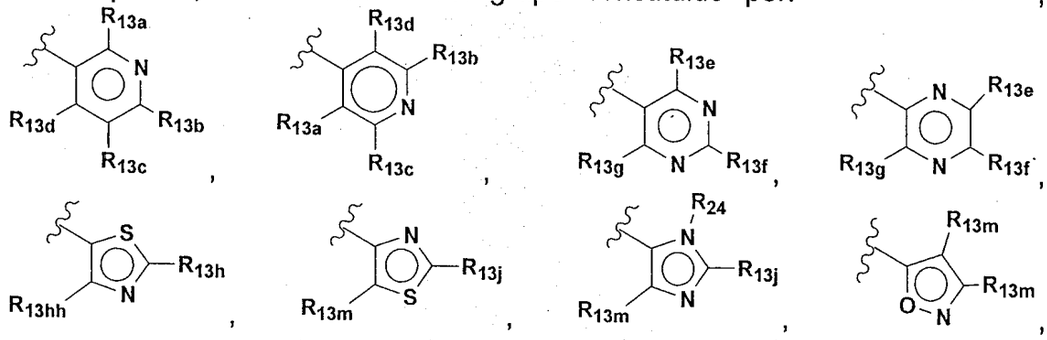
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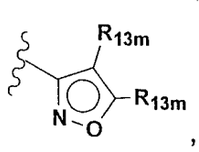
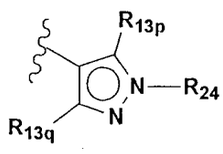


En otra realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I,

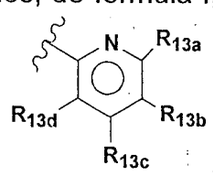


en la que R_1 se selecciona del grupo constituido por:

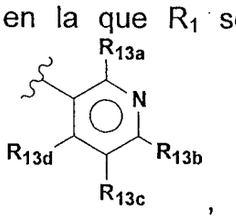
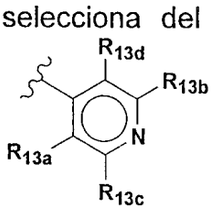
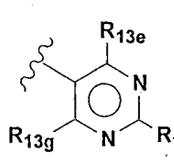
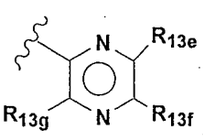


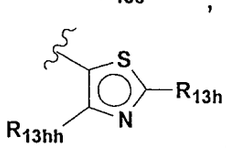
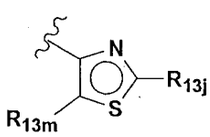
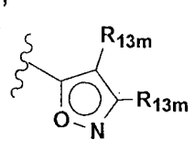
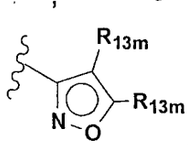

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En otra realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I,

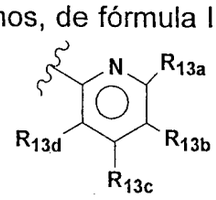

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en la que R_1 se selecciona del grupo constituido por:

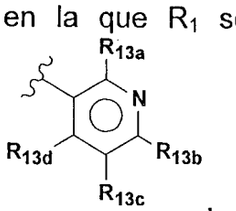
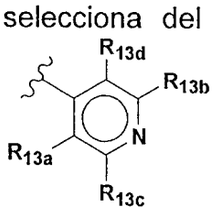
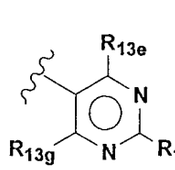
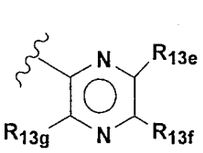

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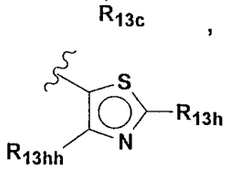
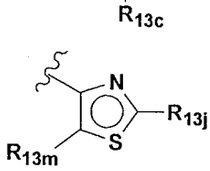
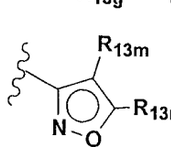

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En una realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I,

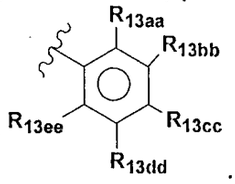

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en la que R_1 se selecciona del grupo constituido por:

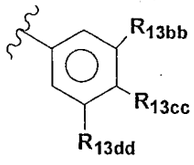

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En una realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I,

en la que R_1 es 

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En una realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que R_1 es 

.

En una realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que:

X es H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Y es H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Z es H, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-}

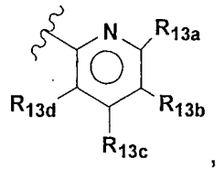
$_{12}$, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 6 a 12 miembros, heterociclilo de 4 a 12 miembros, $-NO_2$, $-SO_2NR_{11}R_{12}$, $-NCOR_{11}$, $-NR_{11}SO_2NR_{11}R_{12}$, $-OCONR_{11}R_{12}$ o $-NR_{11}R_{12}$;

A es $-(CH_2)_m-R_2$, $-CH(R_{25})(R_{26})$ o $-CH(R_{26})-CO_2-R_{2a}$;

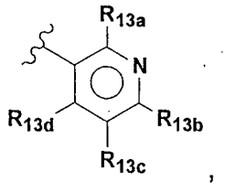
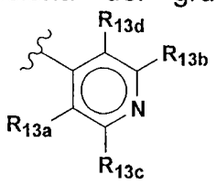
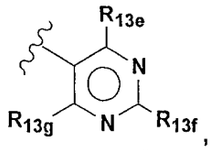
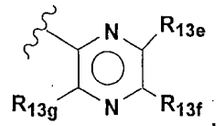
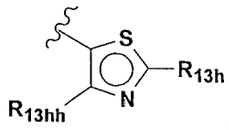
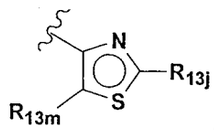
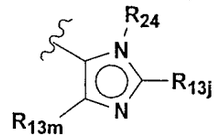
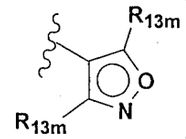
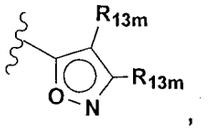
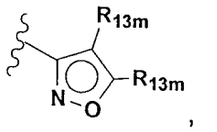
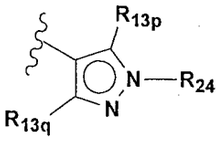
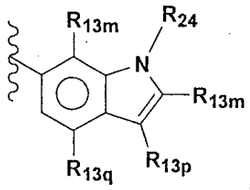
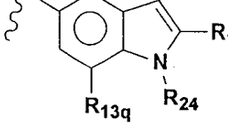
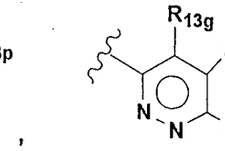
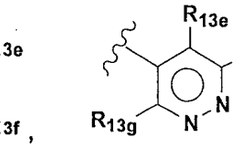
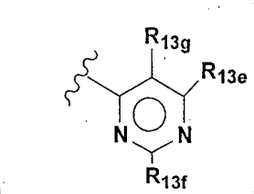
m es 0 a 4;

n es 1 a 4;

R_1 es -OH, F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, cicloalquilo C_{3-10}, -CN, $-(CH_2)_n-SO_2NR_{11}R_{12}$ o $-(CH_2)_n-NR_{11}SO_2R_{12}$, pudiendo estar el alquenilo y cicloalquilo opcionalmente sustituidos con uno o más R_{13}; o



R_1 se selecciona del grupo constituido por:

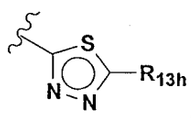
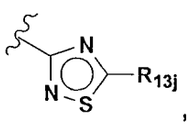
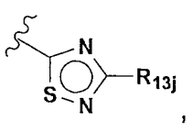
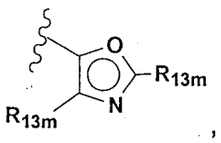
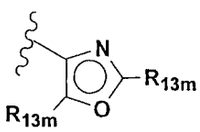
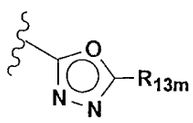
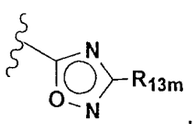
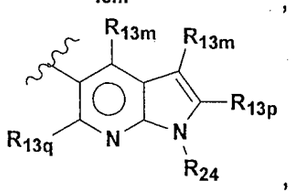
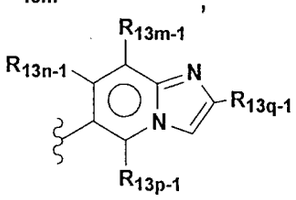
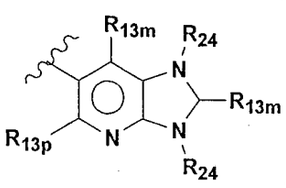
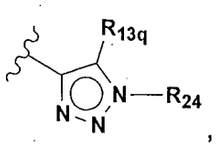
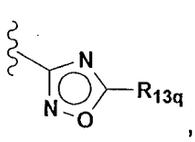
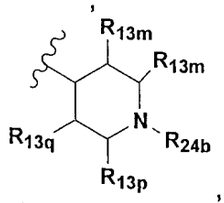
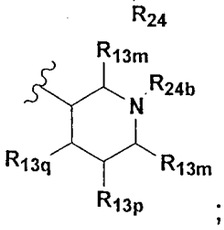
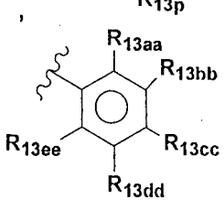

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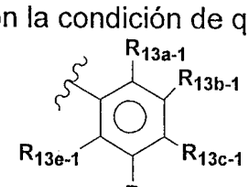
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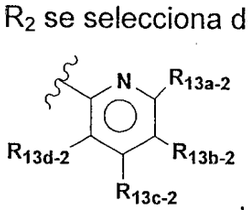
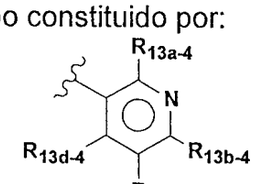
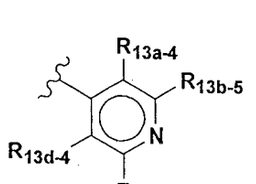
5 R_1 es ;

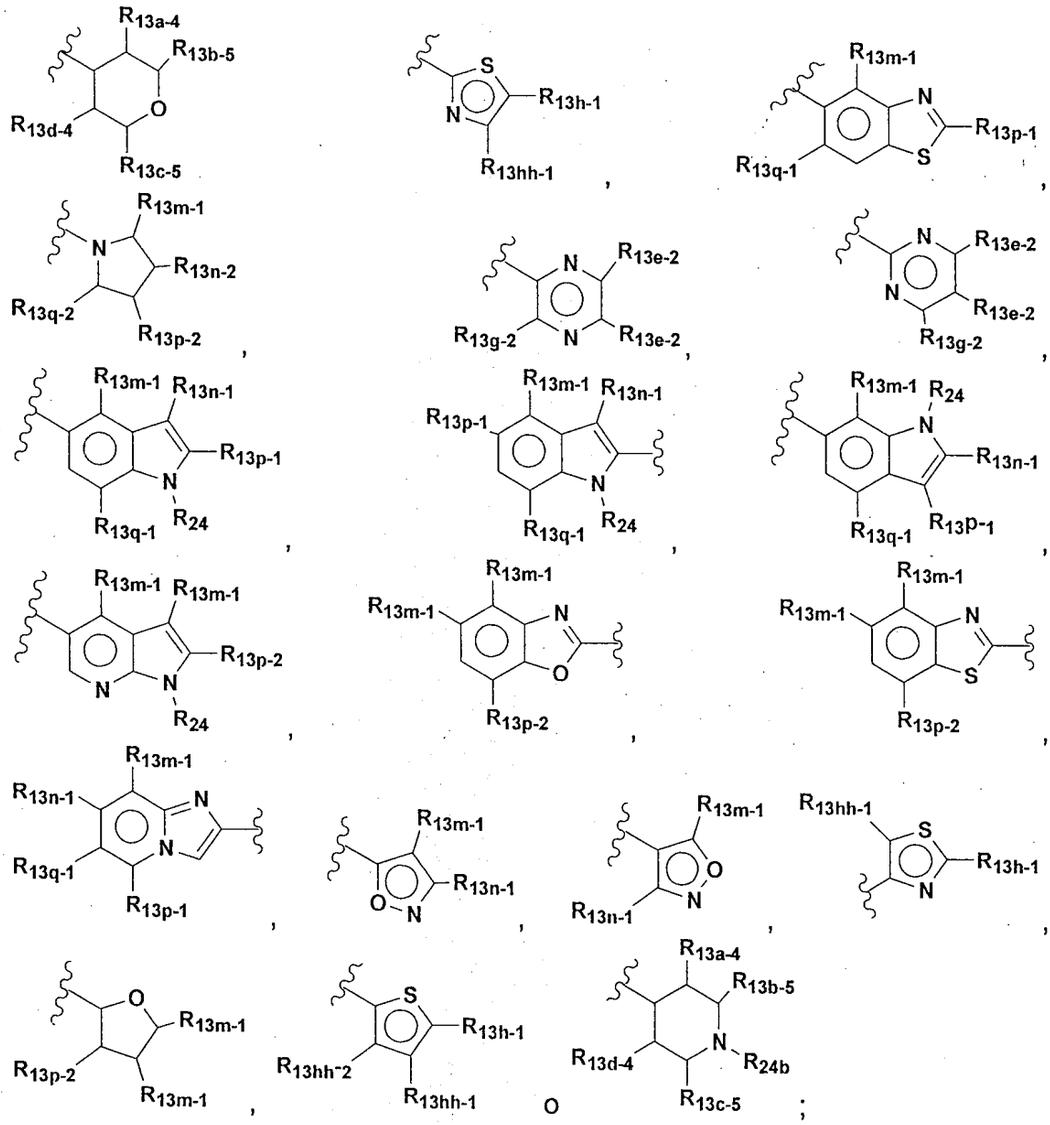
R_2 es alquilo C_{1-10}, ciclopropilo opcionalmente sustituido con uno o más R_{13}; cicloalquilo C_{4-10} opcionalmente sustituido con uno o más R_{13bb}; o $-NR_{14}R_{14}$; con la condición de que R_2 no sea $-NR_{14}R_{14}$ cuando m sea 0, 1 ó 3; o



R_2 es ; o

10 R_2 se selecciona del grupo constituido por:



R_{2a} es alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, $-NR_{14}R_{14}$, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, cualquiera de los cuales está opcionalmente sustituido con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{11} y R_{12}, en cada aparición, se seleccionan independientemente de H, alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros y un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

R_{11} y R_{12} se toman junto con el nitrógeno al que están unidos formando un heterociclilo de 4 a 12 miembros, pudiendo estar el heterociclilo opcionalmente sustituido con uno o más R_{13} y el heterociclilo está constituido por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; con la condición de que cuando R_{13} sea alquilo sustituido con un R_{14a}, R_{14a} no sea -

OH;

R_{13a}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13aa}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2}, en cada aparición, es independientemente H, -OH, F, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I,

alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13bb}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo

C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de

4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, -

$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ o -$CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -CO_2R_{26}, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ o -$CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13cc}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-

$NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 6 a 12 miembros, un heterociclilo de 6 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, $-NO_2$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, -

$NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-4}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo

estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13dd}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo

opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo

están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados

independientemente del grupo constituido por N, S u O;

R_{13ee}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-1}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13f}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I,

alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13h}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12},

alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13h-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{7-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de

4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, -

$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ o -$CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13j}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ o -$CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13m}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-

$NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13m-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13n-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, -

$NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13p}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13p-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, -

$NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13p-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo

estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo

opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{14} se toman junto con los átomos a los que están unidos formando un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-NO_2$, $-CO_2R_{26}$, $-OCONR_{24}R_{24}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-CONR_{24}R_{24}$, $-COR_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$, $-NR_{24}CO_2R_{24}$, $-SO_2NR_{24}R_{24}$, o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y

heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{24} se toman junto con los átomos a los que están unidos formando un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-COR_{25}$, $-NR_{25}R_{25}$, $-NR_{25}CO_2R_{25}$, o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24b}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, $-CO_2R_{25}$, $-SO_2NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados

independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O.

En una realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que:

X es H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Y es H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Z es H, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 6 a 12 miembros, heterociclilo de 4 a 12 miembros, $-NO_2$ o $-NR_{11}R_{12}$;

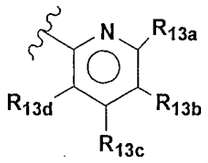
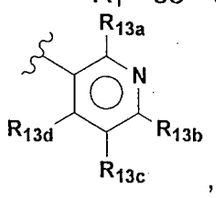
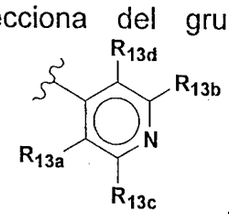
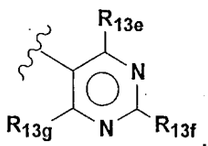
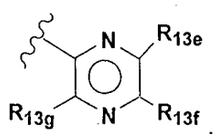
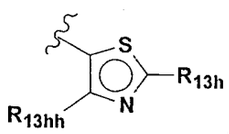
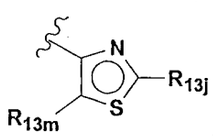
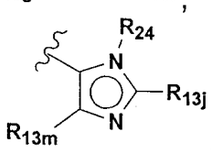
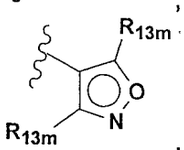
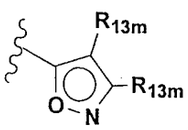
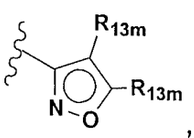
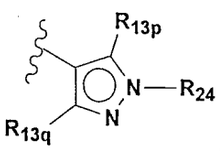
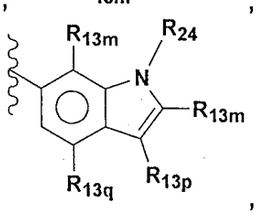
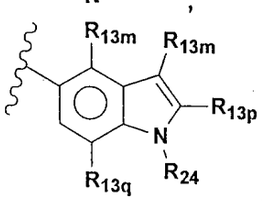
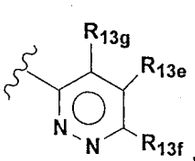
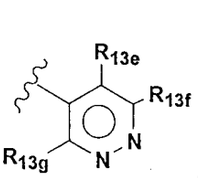
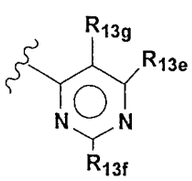
A es $-(CH_2)_m-R_2$ o $-CH(R_{25})(R_{26})$;

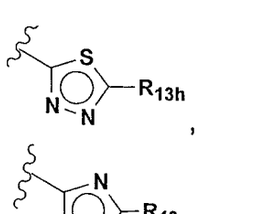
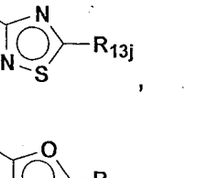
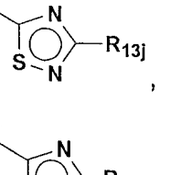
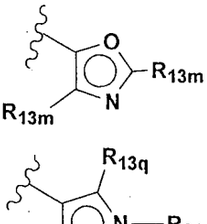
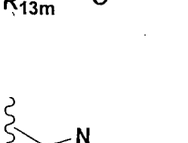
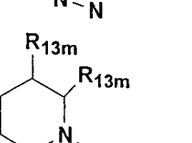
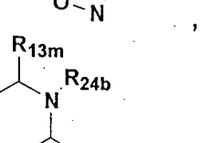
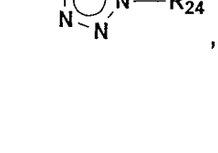
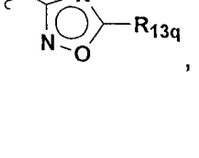
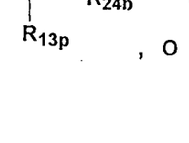
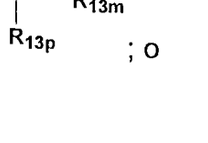
m es 0 a 4;

n es 1 a 4;

R_1 es F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, cicloalquilo C_{3-10}, $-(CH_2)_n-SO_2NR_{11}R_{12}$ o $-(CH_2)_n-NR_{11}SO_2R_{12}$, pudiendo estar el alquenilo y cicloalquilo opcionalmente sustituidos con uno o más R_{13}; o

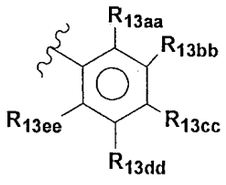
R_1 se selecciona del grupo constituido por:

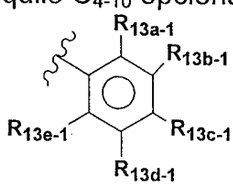
, o

; o



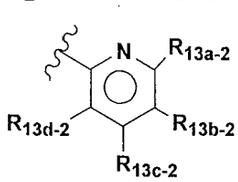
R_1 es ;

R_2 es alquilo C_{1-10}, ciclopropilo opcionalmente sustituido con uno o más R_{13}; o cicloalquilo C_{4-10} opcionalmente sustituido con uno o más R_{13bb}; o



R_2 es ; o

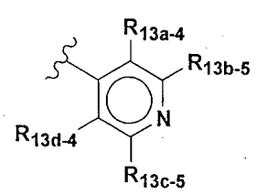
R_2 se selecciona del grupo constituido por:



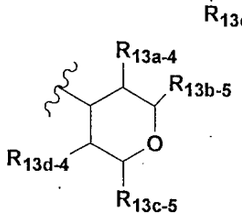
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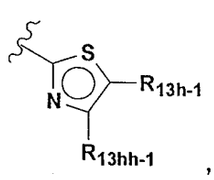


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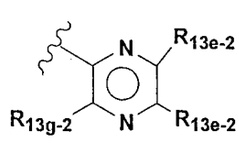


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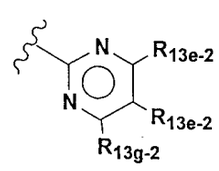




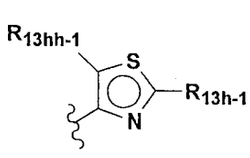
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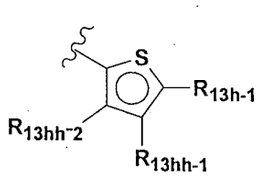
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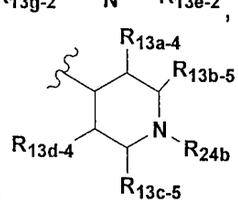


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o ;

R_{11} y R_{12}, en cada aparición, se seleccionan independientemente de H, alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros y un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

R_{11} y R_{12} se toman junto con el nitrógeno al que están unidos formando un heterociclilo de 4 a 12 miembros, pudiendo estar el heterociclilo opcionalmente sustituido con uno o más R_{13} y el heterociclilo está constituido por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; con la condición de que cuando R_{13} sea alquilo sustituido con un R_{14a}, R_{14a} no sea -OH;

R_{13a}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, -

$NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13aa}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-1}, en cada aparición, es independientemente -OH, F, Cl, Br, I, alquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, -

$NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2}, en cada aparición, es independientemente H, -OH, F, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo

estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13bb}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente

sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos

por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos

seleccionados independientemente del grupo constituido por N, S u O;

R_{13c}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13cc}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 6 a 12 miembros, un heterociclilo de 6 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, $-NO_2$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-4}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12},

000652

alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de

4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13dd}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, -

009654

$NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-$

$NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13ee}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, -

$NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-1}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, -

$NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13f}, en cada aparición, es independientemente -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo

estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13h}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo

opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13h-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{7-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo

están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos

seleccionados independientemente del grupo constituido por N, S u O;

R_{13j}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13m}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13p}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno,

alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{14} se toman junto con los átomos a los que están unidos formando un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-NO_2$, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-CONR_{24}R_{24}$, $-COR_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$, $-NR_{24}CO_2R_{24}$, $-SO_2NR_{24}R_{24}$, o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{24} se toman junto con los átomos a los que están unidos formando

un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-COR_{25}$, $-NR_{25}CO_2R_{25}$, o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24b}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, $-CO_2R_{25}$, $-SO_2NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos

seleccionados independientemente del grupo constituido por N, S u O.

En una realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que:

X es H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Y es H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Z es H, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, un heteroarilo de 6 a 12 miembros, heterociclilo de 4 a 12 miembros o $-NR_{11}R_{12}$;

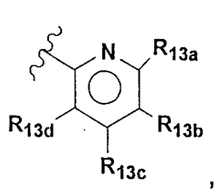
A es $-(CH_2)_m-R_2$ o $-CH(R_{25})(R_{26})$;

m es 0 a 3;

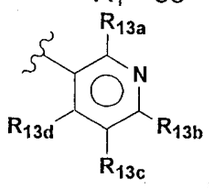
n es 1 a 3;

R_1 es F, Cl, Br, I, alquilo C_{1-10}, alquenilo C_{2-12}, cicloalquilo C_{3-10}, $-(CH_2)_n-SO_2NR_{11}R_{12}$ o $-(CH_2)_n-NR_{11}SO_2R_{12}$, pudiendo estar el alquenilo y cicloalquilo opcionalmente sustituidos con uno o más R_{13}; o

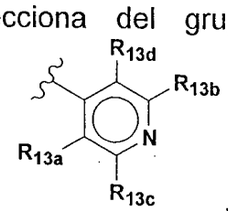
R_1 se selecciona del grupo constituido por:



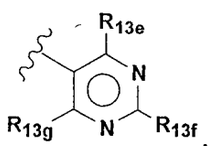
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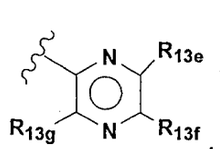
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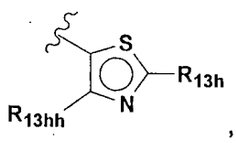
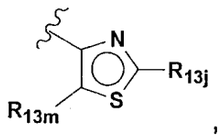
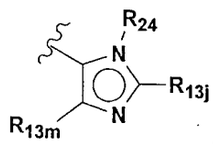
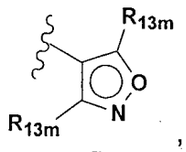
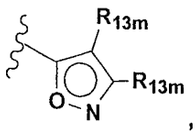
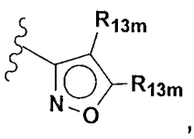
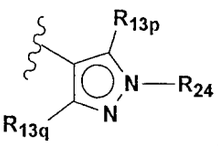
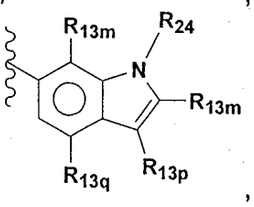
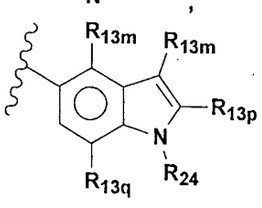
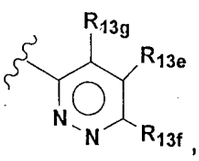
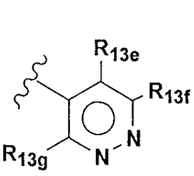
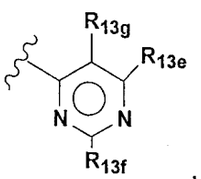
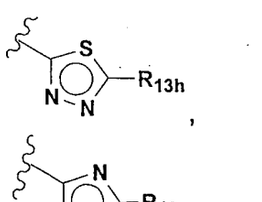
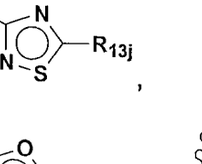
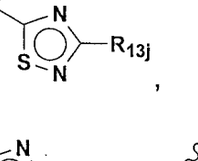
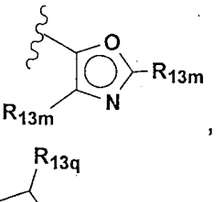
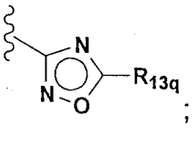
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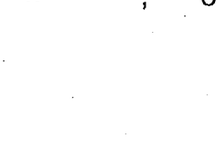
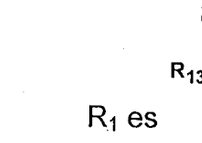
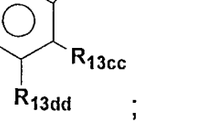


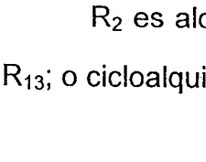
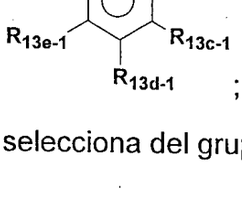
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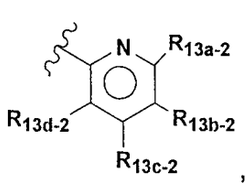
R_1 es ;

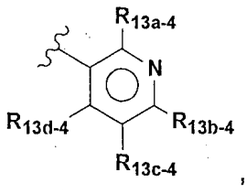
R_2 es alquilo C_{1-10}, ciclopropilo opcionalmente sustituido con uno o más R_{13}; o cicloalquilo C_{4-10} opcionalmente sustituido con uno o más R_{13bb}; o

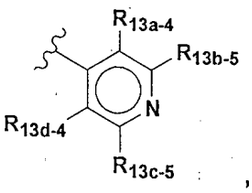


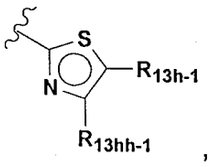
R_2 es ; o

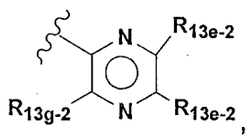
R_2 se selecciona del grupo constituido por:

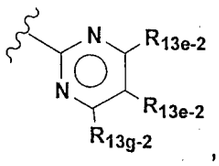


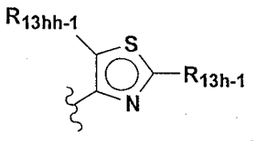
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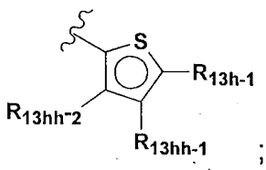
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R_{11} y R_{12}, en cada aparición, se seleccionan independientemente de H, alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros y un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

R_{11} y R_{12} se toman junto con el nitrógeno al que están unidos formando un heterociclilo de 4 a 12 miembros, pudiendo estar el heterociclilo opcionalmente sustituido con uno o más R_{13} y el heterociclilo está constituido por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -

$(CH_2)_m$-SO_2R_{14}, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ o -$NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; con la condición de que cuando R_{13} sea alquilo sustituido con un R_{14a}, R_{14a} no sea -OH;

R_{13a}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ o -$NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13aa}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -

$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ o -$NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, ó -$CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2}, en cada aparición, es independientemente H, -OH, F, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$,

$-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, -

$NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13bb}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, -

$NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y

heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos

por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13cc}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 6 a 12 miembros, un heterociclilo de 6 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, $-NO_2$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-4}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I,

alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13dd}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12},

alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$ o $-CO_2R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, -

$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ o -$NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ o -$NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -

$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ o -$NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13ee}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ o -$NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-1}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -

$SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13f}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o -

$NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo,

alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13h}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13h-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{7-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo

opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de

carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13m}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del

grupo constituido por N, S u O;

R_{13p}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{14} se toman junto con los átomos a los que están unidos formando un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-NO_2$, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-CONR_{24}R_{24}$, $-COR_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{24} se toman junto con los átomos a los que están unidos formando un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-COR_{25}$, $-NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O.

En una realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que:

X es H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10},

heterociclilo de 4 a 12 miembros, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Y es H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, heterociclilo de 4 a 12 miembros, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Z es H, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, heterociclilo de 4 a 12 miembros o $-NR_{11}R_{12}$;

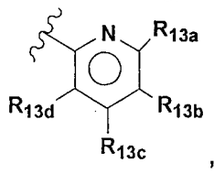
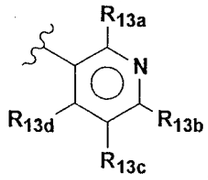
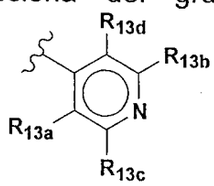
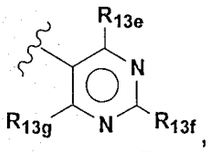
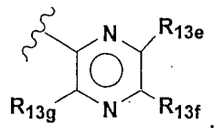
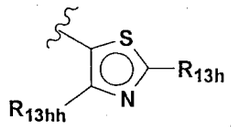
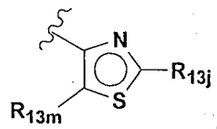
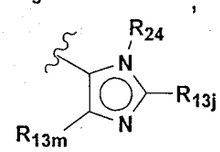
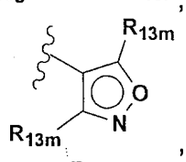
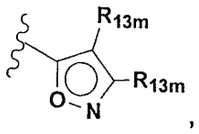
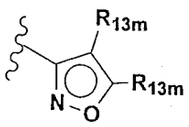
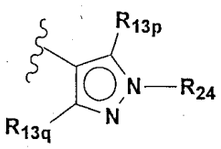
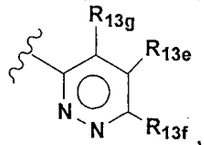
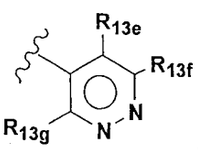
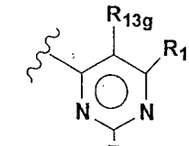
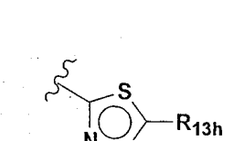
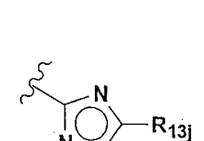
A es $-(CH_2)_m-R_2$;

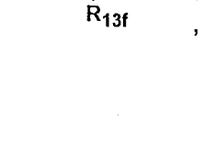
m es 0 a 3;

n es 1 a 3;

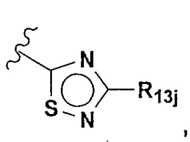
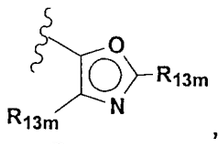
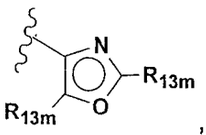
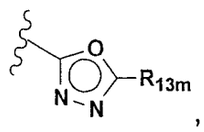
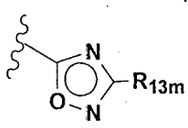
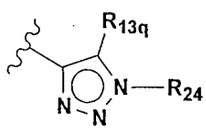
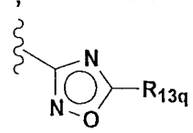
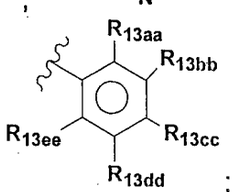
R_1 es F, Cl, Br, I, alquilo C_{1-10}, alquenilo C_{2-12}, cicloalquilo C_{3-10}, pudiendo estar el alquenilo y cicloalquilo opcionalmente sustituidos con uno o más R_{13}; o

R_1 se selecciona del grupo constituido por:

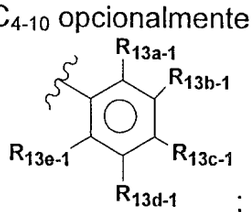



,

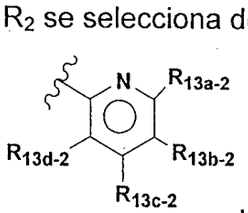
R_1 es ;

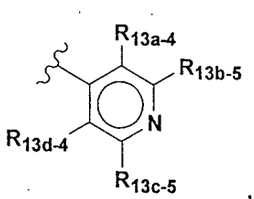
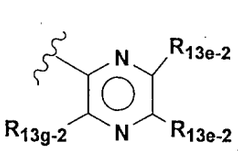
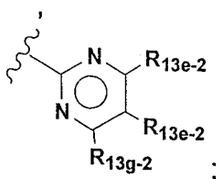
R_2 es ciclopropilo opcionalmente sustituido con uno o más R_{13}; o cicloalquilo C_{4-10} opcionalmente sustituido con uno o más R_{13bb}; o



R_2 es ; o

R_2 se selecciona del grupo constituido por:



;

R_{11} y R_{12}, en cada aparición, se seleccionan independientemente de H, alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros y un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del

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grupo constituido por N, S u O; o

R_{11} y R_{12} se toman junto con el nitrógeno al que están unidos formando un heterociclilo de 4 a 12 miembros, pudiendo estar el heterociclilo opcionalmente sustituido con uno o más R_{13} y el heterociclilo está constituido por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; con la condición de que cuando R_{13} sea alquilo sustituido con un R_{14a}, R_{14a} no sea -OH;

R_{13a}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, -

$SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13aa}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, -

$NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2}, en cada aparición, es independientemente H, -OH, F, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo,

heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13bb}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y

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heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó

4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

000696

R_{13c}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13cc}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12},

arilo C_{6-10}, un heteroarilo de 6 a 12 miembros, un heterociclilo de 6 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-4}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-$

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$NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, -

$NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13dd}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$ o $-CO_2R_{14}$,

pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el

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heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13ee}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó

4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-1}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por

N, S u O;

R_{13f}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13h}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I,

alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13m}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o

un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-CONR_{24}R_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O.

En otra realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que:

X es H, F, Cl, Br, I, alcoxi C_{1-10}, haloalquilo C_{1-10}, heterociclilo de 4 a 12 miembros, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Y es H, F, Cl, Br, I, alcoxi C_{1-10}, haloalquilo C_{1-10}, heterociclilo de 4 a 12 miembros, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

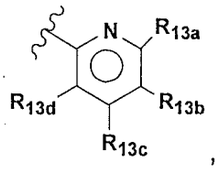
Z es H, Cl, Br, I, alcoxi C_{1-10}, haloalquilo C_{1-10}, heterociclilo de 4 a 12 miembros o $-NR_{11}R_{12}$;

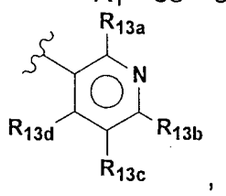
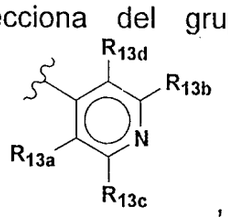
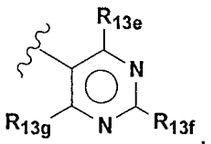
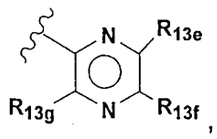
A es $-(CH_2)_m-R_2$;

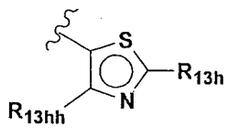
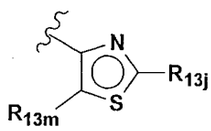
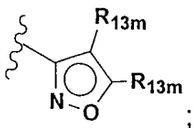
m es 0 a 3;

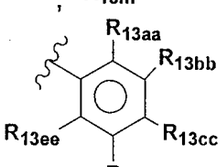
n es 1 a 3;

R_1 es Cl, alquenilo C_{2-12}, cicloalquilo C_{3-10}, pudiendo estar el alquenilo y cicloalquilo opcionalmente sustituidos con uno o más R_{13}; o

R_1 se selecciona del grupo constituido por:  ,

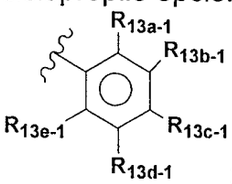
 ,  ,  ,  ,

 ,  o  ; o



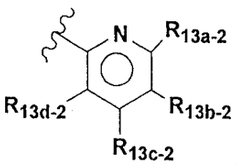
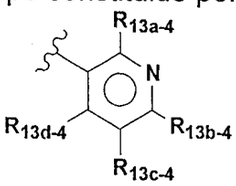
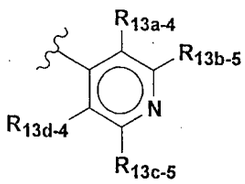
R_1 es ;

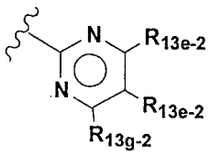
R_2 es ciclopropilo opcionalmente sustituido con uno o más R_{13}; o



R_2 es ; o

R_2 se selecciona del grupo constituido por:

 ,  ,  o

 ;

R_{11} y R_{12}, en cada aparición, se seleccionan independientemente de H, alquilo $C_{1\text{-}10}$, haloalquilo $C_{1\text{-}10}$, cicloalquilo $C_{3\text{-}10}$, arilo $C_{6\text{-}10}$, un heteroarilo de 4 a 12 miembros y un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo,

cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; con la condición de que cuando R_{13} sea alquilo sustituido con un R_{14a}, R_{14a} no sea -OH;

R_{13a}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y

heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13aa}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente

sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2}, en cada aparición, es independientemente H, -OH, F, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó

4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13bb}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N,

009713

S u O;

R_{13b-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

000714

R_{13b-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12},

000715

arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13cc}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 6 a 12 miembros, un heterociclilo de 6 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, $-NR_{14}SO_2R_{14}$, -

000716

$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$ o -$NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ o -$NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-4}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$ o -

$NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo,

heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13dd}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$ o $-CO_2R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo

están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por

009720

N, S u O;

R_{13e}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13ee}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-1}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13f}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I,

alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12},

000723

arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-CONR_{24}R_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno,

000724

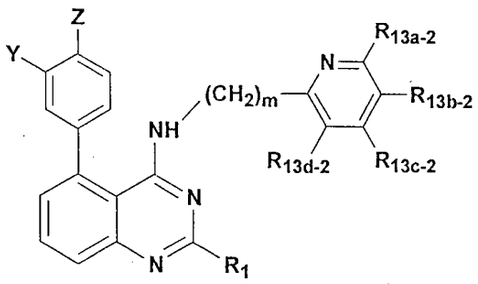
alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

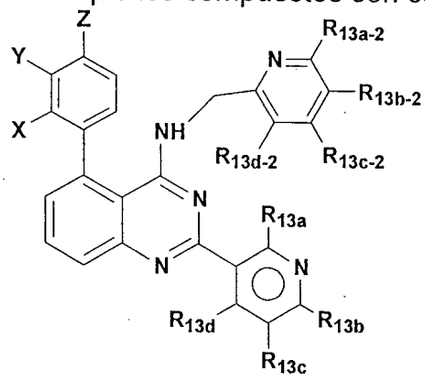
R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O.

En otra realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que los compuestos son compuestos de fórmula Ia:



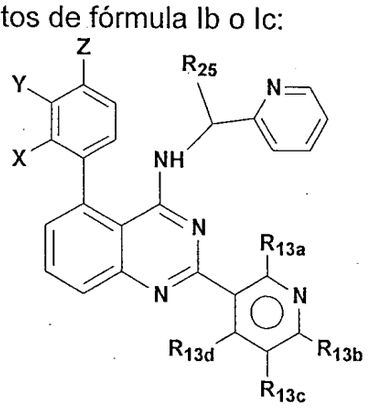
(Ia).

En otra realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula I, en la que los compuestos son compuestos de fórmula Ib o Ic:



Ib

o



Ic

en las que:

X es H, F, Cl, Br, I, alcoxi C_{1-10}, haloalquilo C_{1-10}, heterociclilo de 4 a 12 miembros, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Y es H, F, Cl, Br, I, alcoxi C_{1-10}, haloalquilo C_{1-10}, heterociclilo de 4 a 12 miembros, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Z es H, Cl, Br, I, alcoxi C_{1-10}, haloalquilo C_{1-10}, heterociclilo de 4 a 12 miembros o $-NR_{11}R_{12}$;

R_{11} y R_{12}, en cada aparición, se seleccionan independientemente de H, alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros y un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2} es independientemente H, -OH, F, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$,

pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b} es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-CONR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$ o $-NR_{14}CONR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo

000728

opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c} es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, hidroxialquilo C_{1-10}, cianoalquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-(CH_2)_m-SO_2R_{14}$, $-(CH_2)_n-OCONR_{14}R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$, $-NR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$ o $-NR_{14}CONR_{14}R_{14}$, pudiendo estar el cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, o 3 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4

heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2} es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N,

S u O;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-CO_2H$, $-CO_2R_{26}$, $-OCONR_{24}R_{24}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-CONR_{24}R_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{24} se toman junto con los átomos a los que están unidos formando un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos

seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

con la condición de que X, Y, Z, R_{13a}, R_{13b}, R_{13d}, R_{13a-2}, R_{13b-2}, R_{13c-2} y R_{13d-2} no sean todos H cuando R_{13c} sea $-C(=O)N(C_2H_4OCH_3)_2$, $-SO_2N(C_2H_4OH)_2$.

En otra realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula Ib.

En otra realización más, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula Ib

000732

o Ic, en la que:

X es H, F, Cl, Br, I, alcoxi C_{1-10}, haloalquilo C_{1-10}, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Y es H, F, Cl, Br, I, alcoxi C_{1-10}, haloalquilo C_{1-10}, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Z es H, Cl, Br, I, alcoxi C_{1-10}, haloalquilo C_{1-10} o $-NR_{11}R_{12}$;

R_{11} y R_{12}, en cada aparición, se seleccionan independientemente de H, alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros y un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2} es independientemente H, -OH, F, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-$

$SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b} es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, o $-NR_{14}CONR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo,

heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c} es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, hidroxialquilo C_{1-10}, cianoalquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$, $-NR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$ o $-NR_{14}CONR_{14}R_{14}$, pudiendo estar el cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2 ó 3 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2} es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por

N, S u O;

R_{13d} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2} es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o

un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-CONR_{24}R_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O.

En una realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula Ib o Ic, en la que:

X es H, F, Cl, Br, I, alcoxi C_{1-10} o haloalquilo C_{1-10};

Y es H, F, Cl, Br, I, alcoxi C_{1-10} o haloalquilo C_{1-10};

Z es H, Cl, Br, I, alcoxi C_{1-10} o haloalquilo C_{1-10};

R_{13a} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2} es independientemente H, -OH, F, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b} es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, o $-NR_{14}CONR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el

alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c} es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, hidroxialquilo C_{1-10}, cianoalquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-NR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$ o $-NR_{14}CONR_{14}R_{14}$, pudiendo estar el cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2 ó 3 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-}

$_{10}$, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2} es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14} se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a} se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10},

haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24} se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a} se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25} se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26} se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo

de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O.

En otra realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula Ib o Ic, en la que:

X es H, F, Cl, Br, I, o alcoxi C_{1-10};

Y es H, F, Cl, Br, I, o alcoxi C_{1-10};

Z es H, Cl, Br, I, alcoxi C_{1-10} o haloalquilo C_{1-10};

R_{13a} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-CONR_{14}R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2} es independientemente H, -OH, F, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, $-CONR_{14}R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b} es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, o $-NR_{14}CONR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c} es independientemente H, Cl, Br, I, alquilo C_{1-10}, hidroxialquilo C_{1-10}, cianoalquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-NR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$ o $-NR_{14}CONR_{14}R_{14}$, pudiendo estar el cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo

están constituidos por átomos de carbono y 1, 2, o 3 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-CONR_{14}R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2} es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-CONR_{14}R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo

están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14} se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a} se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4

a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O.

En otra realización más, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula Ib o Ic, en la que:

X es H, F, Cl, Br, I o alcoxi C_{1-10};

Y es H, F, Cl, Br, I o alcoxi C_{1-10};

Z es H, Cl, Br, I o alcoxi C_{1-10};

R_{13a} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10} o -CN, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con

uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2} es independientemente H, -OH, F, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros o un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b} es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}R_{14}$, o $-NR_{14}CONR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros o un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más

R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c} es independientemente H, Cl, Br, I, alquilo C_{1-10}, hidroxialquilo C_{1-10}, cianoalquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-NR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$ o $-NR_{14}CONR_{14}R_{14}$, pudiendo estar el cicloalquilo, alquenilo, alcoxi, arilo y heteroarilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo está constituido por átomos de carbono y 1, 2 ó 3 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente

sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2} es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10} o -CN pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O.

En una realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula Ib

o Ic, en la que:

X es H o alcoxi C_{1-10};

Y es H o alcoxi C_{1-10};

Z es H o alcoxi C_{1-10};

R_{13a}, en cada aparición, es independientemente H o -CN;

R_{13a-2}, en cada aparición, es independientemente H, F, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10} o cicloalquilo C_{3-10}, pudiendo estar el alquilo, cicloalquilo y alcoxi opcionalmente sustituidos con uno o más R_{14a};

R_{13b}, en cada aparición, es independientemente H, alcoxi C_{1-10}, -CN, -$CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$NR_{14}R_{14}$, o -$NR_{14}CONR_{14}R_{14}$;

R_{13b-2}, en cada aparición, es independientemente H o F;

R_{13c}, en cada aparición, es independientemente H, alquilo C_{1-10}, alcoxi C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, un heteroarilo de 4 a 12 miembros, -CN, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -$NR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$ o -$NR_{14}CONR_{14}R_{14}$, pudiendo estar el cicloalquilo, alquenilo, alcoxi y heteroarilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo está constituido por átomos de carbono y 1, 2 ó 3 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2}, R_{13d} y R_{13d-2} son H;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó

4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo

constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O.

En otra realización, se proporcionan compuestos, enantiómeros, diastereómeros, tautómeros, profármacos o sales de los mismos, de fórmula Ib o Ic, en la que:

X, Y, Z, R_{13a}, R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d} y R_{13d-2} son H;

R_{13b}, en cada aparición, es independientemente H, alcoxi C_{1-10}, o -$NR_{14}R_{14}$;

R_{13c}, en cada aparición, es independientemente H, alquilo C_{1-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$CONR_{14}R_{14}$ o -$NR_{14}R_{14}$, pudiendo estar el cicloalquilo y heteroarilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo está constituido por átomos de carbono y 1, 2 ó 3 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por

N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados

independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O.

En otra forma de realización, compuestos, enantiómeros, diaestereómeros, tautómeros, o sales de los mismos, de la presente invención se seleccionan de los compuestos que se ejemplifican en los Ejemplos, preferentemente los Ejemplos 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 y 137, más preferentemente los ejemplos 7, 32 y 101, incluso más preferentemente los Ejemplos 7 y 101.

En una forma de realización, se proporcionan composiciones farmacéuticas que comprenden una cantidad terapéuticamente eficaz de al menos un compuesto de fórmula I, Ia, Ib y/o Ic, preferentemente compuestos ejemplificados en los ejemplos, más preferentemente los Ejemplos 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 y 137, incluso más preferentemente los Ejemplos 7, 32 y 101, todavía más preferentemente los ejemplos 7 y 101.

En otra forma de realización, se proporcionan composiciones farmacéuticas que comprenden una cantidad terapéuticamente eficaz de al menos un compuesto de fórmula I, Ia, Ib y/o Ic, preferentemente compuestos ejemplificados en los ejemplos, más preferentemente los Ejemplos 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 y 137, incluso más preferentemente los Ejemplos 7, 32 y 101, todavía más preferentemente

los ejemplos 7 y 101, y al menos otro agente terapéutico, por ejemplo agentes antiarrítmicos, bloqueantes de los canales de calcio, agentes antiplaquetarios, agentes antihipertensores, agentes antitrombóticos/antitrombolíticos, anticoagulantes, inhibidores de la HMG-CoA reductasa, agentes antidiabéticos, miméticos tiroideos, antagonistas de los receptores de mineralocorticoides y glicósidos cardíacos.

En otra forma de realización más se proporcionan composiciones farmacéuticas que comprenden una cantidad terapéuticamente eficaz de al menos un compuesto de fórmula I, Ia, Ib y/o Ic, preferentemente compuestos ejemplificados en los ejemplos, más preferentemente los Ejemplos 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 y 137, incluso más preferentemente los Ejemplos 7, 32 y 101, todavía más preferentemente los ejemplos 7 y 101, y al menos otro agente terapéutico, por ejemplo sotalol, dofetilida, diltiazem, verapamilo, clopidogrel, cangrelor, ticlopidina, CS-747, ifetroban, aspirina, un bloqueante beta adrenérgico, un inhibidor de la ECA, un antagonista de A II, un antagonista de ET, un antagonista doble de ET/A II, un inhibidor de la vasopeptidasa, tPA, tPA recombinante, TNK, nPA, un inhibidor del factor VIIa, un inhibidor del factor Xa, un inhibidor del factor XIa, un inhibidor de la trombina, warfarina, una heparina, pravastatina, lovastatina, atorvastatina, simvastatina, NK-104, ZD-4522, una biguanida, una combinación de biguanida/gliburida, espironolactona, eplerinona, digitálicos y ouabaína.

En otra forma de realización más, se proporcionan composiciones farmacéuticas que comprenden una cantidad terapéuticamente eficaz de al menos un compuesto de fórmula I, Ia, Ib y/o Ic, preferentemente compuestos ejemplificados en los ejemplos, más preferentemente los Ejemplos 7, 22, 29,

31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 y 137, incluso más preferentemente los Ejemplos 7, 32 y 101, todavía más preferentemente los ejemplos 7 y 101, y al menos otro agente terapéutico, por ejemplo captopril, zofenopril, fosinopril, enalapril, ceranopril, cilazopril, delapril, pentopril, quinapril, ramipril, lisinopril, omapatrilat, gemopatrilat y razaxaban.

En una forma de realización, se proporcionan procedimientos para tratar o prevenir arritmias, que comprenden administrar a un paciente que lo necesite una cantidad eficaz de al menos un compuesto de fórmula I, Ia, Ib y/o Ic, preferentemente compuestos ejemplificados en los ejemplos, más preferentemente los Ejemplos 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 y 137, incluso más preferentemente los Ejemplos 7, 32 y 101, todavía más preferentemente los ejemplos 7 y 101.

En otra forma de realización, se proporcionan procedimientos para tratar o prevenir arritmias supraventriculares, por ejemplo fibrilación auricular y aleteo auricular, que comprenden administrar a un paciente que lo necesite una cantidad eficaz de al menos un compuesto de fórmula I, Ia, Ib y/o Ic, preferentemente compuestos ejemplificados en los ejemplos, más preferentemente los Ejemplos 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 y 137, incluso más preferentemente los Ejemplos 7, 32 y 101, todavía más preferentemente los ejemplos 7 y 101.

En una forma de realización, se proporciona un procedimiento de controlar la frecuencia cardíaca, que comprende administrar a un paciente que lo necesite una cantidad eficaz de al menos un compuesto de fórmula I, Ia, Ib y/o Ic, preferentemente compuestos ejemplificados en los ejemplos, más preferentemente los Ejemplos 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105,

107, 108, 110, 111, 130, 134 y 137, incluso más preferentemente los Ejemplos 7, 32 y 101, todavía más preferentemente los ejemplos 7 y 101.

En otra forma de realización, se proporcionan procedimientos para tratar una afección asociada con la I_{Kur}, por ejemplo trastornos gastrointestinales, tales como esofagitis por reflujo y un trastorno de la motilidad, enfermedades inflamatorias y/o inmunológicas, tales como enfermedad pulmonary obstructiva crónica, diabetes, trastornos cognitivos, migrañas, epilepsia e hipertensión, que comprenden administrar a un paciente que lo necesite una cantidad eficaz de al menos un compuesto de fórmula I, Ia, Ib y/0 Ic, preferentemente compuestos ejemplificados en los ejemplos, más preferentemente los Ejemplos 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 y 137, incluso más preferentemente los Ejemplos 7, 32 y 101, todavía más preferentemente los ejemplos 7 y 101.

La invención puede estar contemplada en otras formas específicas sin desviarse del espíritu o las características esenciales de la misma. La presente invención también abarca todas las combinaciones de aspectos alternativos de la invención indicada en la presente memoria descriptiva. Se entiende que todas y cada una de las formas de realización de la presente invención pueden tomarse junto con cualquier otra forma de realización para describir formas de realización adicionales de la presente invención. Además, todos los elementos de una forma de realización se pueden combinar con todos y cada uno de los elementos de cualquiera de las formas de realización para describir formas de realización adicionales.

SÍNTESIS

Los compuestos de la presente invención se pueden preparar mediante una serie de modos conocidos para el experto en la técnica de la síntesis orgánica. Los compuestos de la presente invención se pueden sintetizar usando los procedimientos descritos más adelante, junto con los procedimientos sintéticos conocidos en la técnica de química orgánica sintética, o mediante variaciones de las mismas tal como las aprecian los expertos en la técnica. Procedimientos preferidos incluyen, entre otros, los que se describen más adelante. Las reacciones se realizan en un disolvente o mezcla de disolventes adecuados para los reactivos y materiales empleados, y adecuados para las transformaciones que se efectúan. Los expertos en la técnica de la síntesis orgánica entenderán que la funcionalidad presente en la molécula debe ser compatible con las transformaciones propuestas. En ocasiones esto requerirá juicio para modificar el orden de las etapas sintéticas o para seleccionar un esquema de procedimiento concreto por encima de otro con el fin de obtener un compuesto de la invención deseado.

Los nuevos compuestos de la presente invención se pueden preparar usando las reacciones y técnicas descritas en esta sección. Asimismo, en la descripción de los procedimientos sintéticos descritos más adelante, debe entenderse que todas las condiciones de reacción propuestas, incluidos la elección del disolvente, la atmósfera de la reacción, la temperatura de la reacción, la duración del experimentos y los procedimientos de trabajo, se escogen condiciones estándar para dicha reacción, que un experto en la técnica reconocerá fácilmente. Las restricciones de los sustituyentes que son compatibles con las condiciones de la reacción serán fácilmente evidentes

para un experto en la técnica y se deben usar procedimientos alternativos.

Los compuestos de la presente invención pueden prepararse mediante los procedimientos de ejemplo descritos en los esquemas siguientes y los ejemplos de trabajo, así como los procedimientos relevantes publicados en la literatura que usa un experto en la técnica. Reactivos y procedimientos ejemplares para estas reacciones aparecen en el presente documento a continuación en los ejemplos de trabajo. La protección y desprotección de los grupos funcionales en los procedimientos siguientes pueden llevarse a cabo mediante procedimientos conocidos generalmente en la técnica (véase, por ejemplo, Greene, T.W. y col., *Protecting Groups in Organic Synthesis*, 3ª Ed., Wiley (1999). Procedimientos generales de síntesis orgánicas y transformaciones de grupos funcionales se encuentran en: Trost, B.M. y col., eds., *Comprehensive Organic Synthesis: Selectivity, Strategy & Efficiency in Modern Organic Chemistry*, Pergamon Press, New York, NY (1991); March, J., *Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, 4ª Ed., Wiley & Sons, New York, NY (1992); Katritzky, A.R. y col., eds., *Comprehensive Organic Functional Groups Transformations*, 1ª Ed., Elsevier Science Inc., Tarrytown, NY (1995); Larock, R.C., *Comprehensive Organic Transformations*, VCH Publishers, Inc., New York, NY (1989); y las referencias contenidas en ellos.

Un experto en la técnica puede seleccionar fácilmente disolventes, temperaturas, presiones y otras condiciones de la reacción. Los materiales de partida están disponibles comercialmente o pueden ser preparados con facilidad por un experto en la técnica usando procedimientos conocidos. Para todos los esquemas y compuestos descritos más adelante, Y, Z, A, R_1 y R_{24}

son como se ha descrito para un compuesto de Fórmula (I).

A continuación se indican las definiciones de los símbolos usados a lo largo de los Esquemas 1 a 3 y en los ejemplos:

Me = Metilo

Et = Etilo

Pr = Propilo

i-Pr = Isopropilo

Bu = Butilo

i-Bu = Isobutilo

t-Bu = *terc*-butilo

Ph = Fenilo

Bn = Bencilo

Boc = t*erc*-butiloxicarbonilo

AcOH o HOAc = ácido acético

$AlCl_3$ = cloruro de aluminio

CH_2Cl_2 = Diclorometano

CH_3CN o CAN = Acetonitrilo

$CDCl_3$ = deutero-cloroformo

$CHCl_3$ = Cloroformo

mCPBA o m-CPBA = ácido *meta*-cloroperbenzoico

Cs_2CO_3 = carbonato de cesio

DCM = Diclorometano

DEA = Dietilamina

DIC = Diisopropilcarbodiimida

dil = diluido

DIPEA o base de Hunig = Diisopropiletilamina

DME = 1,2-dimetoxietano

DMF = Dimetilformamida

DMSO = dimetilsulfóxido

ADNc= ADN complementario

EDC = *N*-(3-dimetilaminopropil)-*N'*-etilcarbodiimida

EDTA = ácido etilendiaminotetraacético

Et_3N o TEA = Trietilamina

EtOAc = acetato de etilo

Et_2O = Éter dietílico

EtOH = Etanol

eq = equivalentes

HCl = ácido clorhídrico

HOBt = 1-hidroxibenzotriazol

HAUT = (hexafluorofosfato de 2-(7-aza-1H-benzotriazol-1-il)-1,1,3,3-tetrametiluronio)

H_2SO_4 = ácido sulfúrico

K_2CO_3 = carbonato de potasio

KOAc = acetato de potasio

K_3PO_4 = fosfato de potasio

GS= Grupo saliente

LiOH = hidróxido de litio

MeOH = metanol

min = minuto o minutos

$MgSO_4$ = sulfato de magnesio

MsOH o MSA = ácido metilsulfónico

NaCl = cloruro sódico

NaH = hidruro de sodio

$NaHCO_3$ = bicarbonato de sodio

Na_2CO_3 = carbonato de sodio

NaOH = hidróxido sódico

Na_2SO_3 = sulfito sódico

Na_2SO_4 = sulfato sódico

NH_3 = Amoniaco

NH_4Cl = cloruro amónico

NH_4OH = hidróxido amónico

$Pd(OAc)_2$ = acetato de paladio (II)

Pd/C = paladio sobre carbó

$Pd(dppf)Cl_2$ = [1,1'-bis(difenilfosfino)-ferroceno]dicloropaladio (II)

Ph_3PCl_2 = dicloruro de trifenilfosfina

$Pd(TRIPHENYLPHOSPHINE)_2Cl_2$ = cloruro de bis(trifenilfosfino)paladio (II)

GP = grupo protector

$POCl_3$ = oxicloruro de fósforo

i-PrOH o IPA = Isopropanol

PS = Poliestireno

PyBOP = hexafluorofosfato de (benzotriazol-1-iloxi)tripirrolidinofosfonio

PyBrop = Hexafluorofosfato de bromo-tris-pirrolidino fosfonio

SiO_2 = óxido de silicio

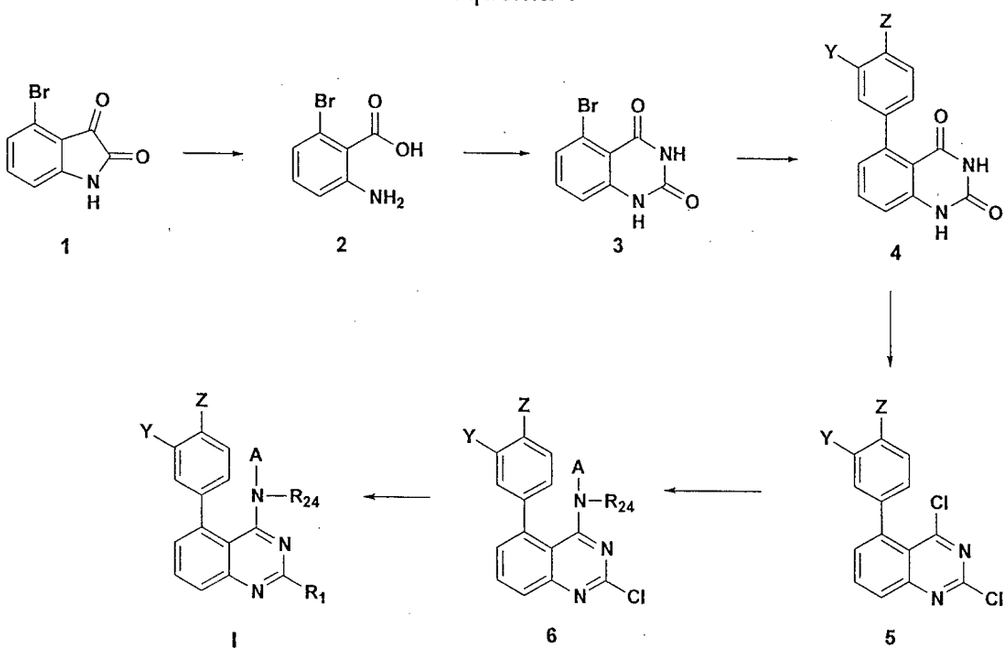
$SnCl_2$ = cloruro de estaño (II)

TFA = ácido trifluoroacético

THF = tetrahidrofurano

TOSMIC = Isocianuro de toluenosulfonilmetilo

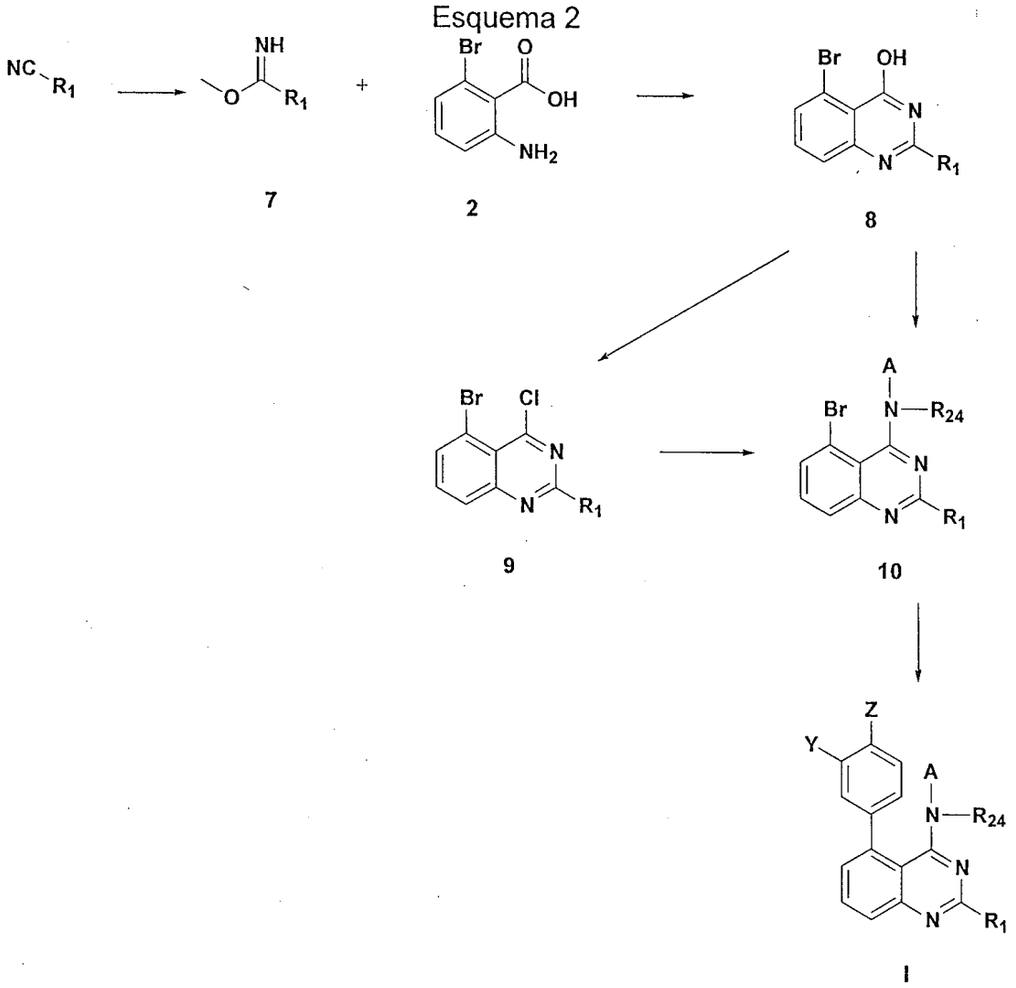
Esquema 1



Los compuestos de fórmula I se pueden sintetizar de acuerdo con el Esquema 1. La 4-bromoindolin-2,3-diona disponible comercialmente se puede hidrolizar a 2-amino-6-bromobenzamida seguida por condensación con isocianato de sodio para formar 5-bromoquinazolin-2,4(1H,3H)-diona. Los protocolos incluyen, entre otros, acoplamiento cruzado mediado por paladio entre 5-bromoquinazolina-2,4(1H,3H)-diona y el ácido arilborónico o éster para formar el intermedio quinazolina-2,4(1H,3H)-diona 5-sustituida. La conversión en la correspondiente dicloro quinazolina y el desplazamiento secuencial en la posición 4, seguido por el acoplamiento cruzado mediado por un metal de transición o desplazamiento de de cloruro C_2 forma compuestos I tal como se

ha descrito.

Esquema 2

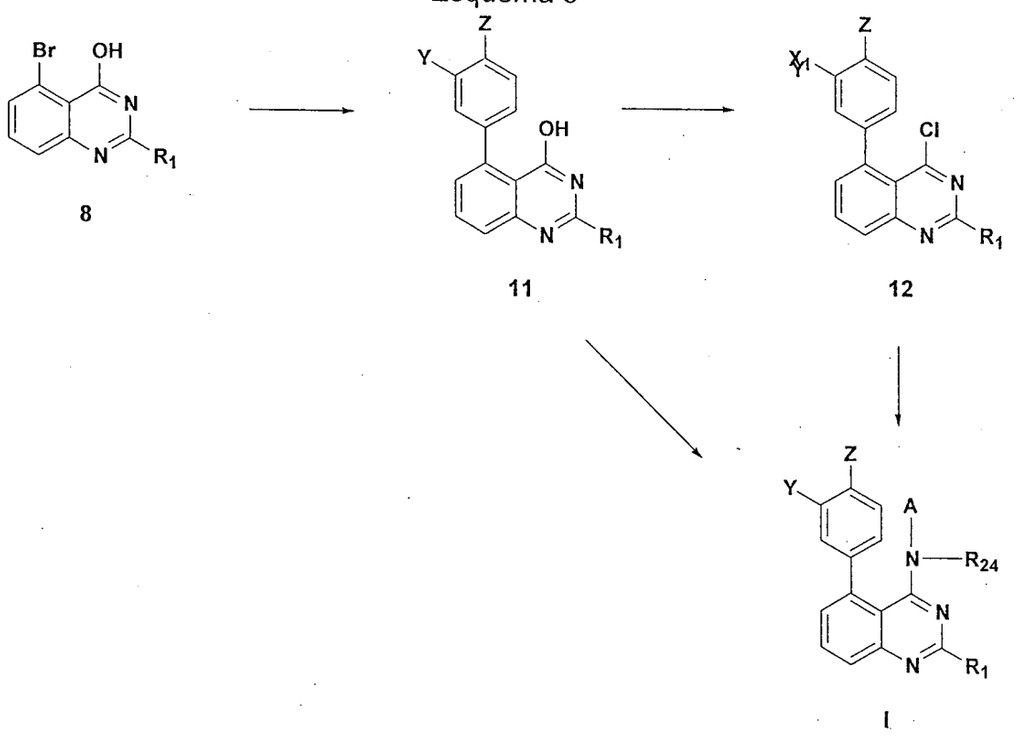


Como alternativa, los compuestos de fórmula I pueden también sintetizarse de acuerdo con el Esquema 2. La formación de carbimidato de metilo a partir del correspondiente nitrilo y la posterior condensación con 2-amino-6-bromobenzamida proporciona compuestos de fórmula **8**. La posterior conversión de **8** en 4-cloroquinazolina intermedia **9** y el desplazamiento del cloruro proporciona 5-bromoquinazolina **10**. Los compuestos de fórmula **10**

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pueden obtenerse directamente a partir de **8** utilizando reactivos de acoplamiento, por ejemplo, entre otros, PyBOP en disolventes adecuados. Los protocolos incluyen, entre otros, acoplamiento cruzado mediado por paladio entre la quinazolina **10** y un ácido o éster arilborónico obteniendo los compuestos de fórmula I.

Esquema 3



Como alternativa, los compuestos de fórmula I pueden también sintetizarse de acuerdo con el Esquema 3. Los compuestos de fórmula **8** pueden someterse a condiciones de acoplamiento cruzado, por ejemplo, entre otros, acoplamiento cruzado mediado por paladio de ácidos o ésteres arilborónicos, seguido por la posterior conversión a la quinazolina intermedia **12** y el desplazamiento del grupo cloro de C_4 obteniendo compuestos de

Fórmula I.

Debe reconocerse que los esquemas anteriores son sólo ilustraciones de algunas vías sintéticas generales para preparar compuestos de la presente invención. Los detalles experimentales para la síntesis de varios ejemplos específicos de la presente invención se describirán más en los ejemplos indicados más adelante. Manipulaciones adicionales de grupos funcionales de los compuestos obtenidos en los esquemas anteriores usando procedimientos conocidos en la técnica deberán proporcionar compuestos adicionales de la presente invención.

EJEMPLOS

Los ejemplos siguientes se ofrecen para ilustrar, pero no limitar, algunas de las formas de realización preferidas de la presente invención y no están destinados a limitar el alcance de la invención. Las abreviaturas y los símbolos químicos tienen sus significados normales y habituales a menos que se indique lo contrario. A menos que se indique lo contrario, los compuestos descritos en la presente memoria descriptiva se han preparado, aislado y caracterizado usando los esquemas y otros procedimientos divulgados en la presente memoria descriptiva o se pueden preparar usando los mismos.

Procedimientos generales

Los procedimientos siguientes se usaron en los Ejemplos de trabajo, a excepción de si se indica lo contrario.

Los procedimientos analíticos de HPLC y HPLC/EM empleados en la

caracterización de los ejemplos son los siguientes:

La HPLC/EM analítica de fase inversa se realizó en sistemas Shimadzu LC10AS acoplados con espectrómetros de masas Waters ZMD (procedimientos A-C, E y F) o el sistema Waters AQUITY® acoplado con un espectrómetros de masas Waters MICROMASS® ZQ (procedimiento D). La CL analítica quiral se realizó en un instrumento Berger Analytical SFC (procedimiento G).

Procedimiento A:

Gradiente lineal de 0 a 100% B durante 2 min, con 3 min a 100% B;

Visualización UV a 220 nm;

Columna: PHENOMENEX® Luna C18 4,6 x 30 mm;

Caudal: 5 ml/min;

Disolvente A: 0,1% de ácido trifluoroacético, 90% de agua, 10% de acetonitrilo;

Disolvente B: 0,1% de ácido trifluoroacético, 90% de acetonitrilo, 10% de agua;

Procedimiento B:

Gradiente lineal de 0 a 100% B durante 10 min, con 5 min a 100% B;

Visualización UV a 220 nm;

Columna: Xbridge fenilo 4,6 x 150 mm;

Caudal: 1 ml/min;

Disolvente A: 0,1% de ácido trifluoroacético, 90% de agua, 10% de acetonitrilo;

Disolvente B: 0,1% de ácido trifluoroacético, 90% de acetonitrilo, 10% de agua;

Procedimiento C:

Gradiente lineal de 0 a 100% B durante 4 min, con 1 min a 100% B;

Visualización UV a 220 nm;

Columna: PHENOMENEX® Luna C18 4,6 x 50 mm;

Caudal: 4 ml/min;

Disolvente A: Acetato amónico 10 mM, 90% de agua, 10% de metanol-,

Disolvente B: Acetato amónico 10 mM, 90% de metanol, 10% de agua.

Procedimiento D:

Gradiente lineal de 2 a 98% B durante 1 min, con 0,5 min a 98% B;

Visualización UV a 220 nm;

Columna: Waters BEH C18 2,1 x 50 mm;

Caudal: 0,8 ml/min;

Disolvente A: 0,05% de TFA, 100% de agua;

Disolvente B: 0,05% de TFA, 100% de ACN;

Procedimiento E:

Gradiente lineal de 0 a 100% B durante 4 min, con 1 min tiempo de retención a 100% B;

Visualización UV a 220 nm;

Columna: Ascentis Express 4,6 x 50 C18 a 45 °C;

Caudal: 4 ml/min;

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Disolvente A: Acetato amónico 10 mM, 5% de ACN, 95% de agua;

Disolvente B: Acetato amónico 10 mM, 95% de ACN, 5% de agua.

Procedimiento F:

Gradiente lineal de 0 a 100% B durante 8 min, con 1 min a 100% B;

Visualización UV a 220 nm;

Columna: PHENOMENEX® Luna C18 4,6 x 75 mm;

Caudal: 2,5 ml/min;

Disolvente A: Acetato amónico 10 mM, 90% de agua, 10% de metanol-,

Disolvente B: Acetato amónico 10 mM, 90% de metanol, 10% de agua.

Procedimiento G:

Isocrático 80/20 de CO_2/MeOH que contiene 0,1% de DEA;

Visualización UV a 220 nm;

Columna: CHIRALPAK® AC, 250 x 4,6 mm, 10 uM;

Caudal: 3,0 ml/min.

Los procedimientos de HPLC preparativa empleados en la purificación de los ejemplos son los siguientes:

Procedimiento H:

Gradiente lineal de 0 a 100% B durante 10 min, con 5 min tiempo de retención a 100% B;

Bombas binarias Shimadzu LC-8A ;

Espectrómetro de masas Waters ZQ usando el software Waters Masslynx 4.0

SP4 EM;

Visualización UV a 220 nm;

Columna: Waters SunFire 19 x 100 mm 5 um C18;

Caudal: 20 ml/min;

Registro de picos por espectrometría de masas;

Disolvente A: 0,1% de TFA, 10% de ACN, 90% de agua;

Disolvente B: 0,1% de TFA, 90% de ACN, 10% de agua.

Procedimiento I:

Gradiente lineal de 20 a 100% B durante 10 min, con 5 min tiempo de retención a 100% B;

Bombas binarias Shimadzu LC-8A ;

Detector de UV Shimadzu SPD-20A;

Visualización UV a 220 nm;

Columna: PHENOMENEX® Luna AXIA 21,1 x 100 mm 5 um C18;

Caudal: 20 ml/min;

Registro de picos por absorbancia en UV;

Disolvente A: 0,1% de TFA, 10% de MeOH, 90% de agua;

Disolvente B: 0,1% de TFA, 90% de MeOH, 10% de agua;

Procedimiento J:

Gradiente lineal de 20 a 100% B durante 10 min, con 2 min tiempo de retención a 100% B;

Bombas binarias Shimadzu LC-8A ;

Detector de UV Shimadzu SPD-10A;

000772

Visualización UV a 220 nm;

Columna: PHENOMENEX® Luna AXIA 21,1 x 100 mm 5 um C18;

Caudal: 20 ml/min;

Registro de picos por absorbancia en UV;

Disolvente A: 0,1% de TFA, 10% de ACN, 90% de agua;

Disolvente B: 0,1% de TFA, 90% de ACN, 10% de agua.

Procedimiento K:

Isocrático 80/20 de CO_2/CH_3OH que contiene 0,1% de DEA;

Instrumento Berger Multigram II SFC;

Visualización UV a 220 nm;

Columna: CHIRALPAK® AD-H 250 x 21 cm ID, 5 uM;

Caudal: 65 ml/min;

Registro de picos por absorbancia en UV.

Los procedimientos analíticos adicionales de HPLC y HPLC/EM empleados en la caracterización de los ejemplos son los siguientes:

Procedimiento L:

Disolvente A- 5% de ACN, 95% de agua, NH_4OAc 10 mM;

Disolvente B- 95% de ACN, 5% de agua, NH_4OAc 10 mM;

Caudal: 4,0 ml/min;

Columna: Ascentis Express C18 (4,6 X 50 cm) mm, 2,7 um;

Tiempo (min): Gradiente %B 0-4,0: 0-100.

Procedimiento M:

Gradiente lineal de 0 a 100% de B durante 2 min;

Visualización UV a 220 nm;

Columna: PHENOMENEX® Luna C18 4,6 x 30 mm;

Caudal: 5 ml/min;

Disolvente A: 0,1% de ácido trifluoroacético, 90% de agua, 10% de metanol;

Disolvente B: 0,1% de ácido trifluoroacético, 90% de metanol, 10% de agua;

Procedimiento N:

Gradiente lineal de 0 a 5% de B durante 0,25 min, después de 5 a 100% de B hasta 2 min con 0,5 min de tiempo de retención a 100% de B;

Visualización UV a 220 nm;

Columna: BEH C18 50 x 2,1 mm – 1,7 µm;

Caudal: 0,6 ml/min;

Disolvente A: 0,1% de ácido fórmico, 95% de agua, 5% de acetonitrilo;

Disolvente B: 0,1% de ácido fórmico, 95% de acetonitrilo, 5% de agua.

Procedimiento O:

Gradiente lineal de 0 a 100% de B durante 2 min;

Visualización UV a 220 nm;

Columna: CHROMOLITH® SpeedROD C18 4,6 x 30 mm;

Caudal: 5 ml/min;

Disolvente A: 0,1% de ácido trifluoroacético, 90% de agua, 10% de metanol;

Disolvente B: 0,1% de ácido trifluoroacético, 90% de metanol, 10% de agua;

Procedimiento P:

Gradiente lineal de 40 a 95% B durante 3 min, con 3 min tiempo de retención a 95% de B;

Visualización UV a 220 nm;

Columna: Atlantis dC18 C18 50 x 4,6 mm - 5 µm;

Caudal: 1,5 ml/min;

Disolvente A: 0,1% de ácido fórmico en agua;

Disolvente B: acetonitrilo.

Procedimiento Q:

Gradiente lineal de 0 a 100% de B durante 2 min;

Visualización UV a 220 nm;

Columna: PHENOMENEX® Luna C18 4,6 x 30 mm;

Caudal: 5 ml/min;

Disolvente A: Acetato amónico 10 mM, 90% de agua, 10% de metanol-,

Disolvente B: Acetato amónico 10 mM, 90% de metanol, 10% de agua.

Procedimiento R:

Gradiente lineal de 30 a 95% B durante 1 min, con 3 min tiempo de retención a 95% de B;

Visualización UV a 220 nm;

Columna: Atlantis dC18 C18 50 x 4,6 mm - 5 µm;

Caudal: 1 ml/min;

Disolvente A: Acetato amónico 10 mM en agua;

Disolvente B: acetonitrilo.

Procedimiento S:

Gradiente lineal de 40 a 95% B durante 3 min, con 1 min tiempo de retención a 95% de B;

Visualización UV a 220 nm;

Columna: Atlantis dC18 C18 50 x 4,6 mm - 5 µm;

Caudal: 1,5 ml/min;

Disolvente A: Acetato amónico 10 mM en agua;

Disolvente B: acetonitrilo.

Procedimiento T:

Gradiente lineal de 0 a 100% de B durante 2 min

Sistemas de la serie Agilent 1200 acoplados con DADetector usando Agilent chemstation y usando software Chemstation B.04.01 (482) con fuente de ionización ESI solo en modo positivo.

Visualización UV a 220 nm;

Columna: Agilent Zorbax SB C18 4,6 x 50 mm 5 um

Programa de Gradiente: Tiempo (min)/%B: 0/0,2/100,3/0.

Caudal: 5,0 ml/min;

Tampón: 0,1% de ácido trifluoroacético en agua.

Fase móvil A: Tampón: Metanol: 90:10

Fase móvil B: Tampón: Metanol: 10:90

Procedimiento U:

Gradiente lineal de 0 a 100% de B durante 2 min;

Visualización UV a 220 nm;

Columna: Chromolith SpeedROD C18 4,6 x 30 mm;

Caudal: 5 ml/min;

Disolvente A: 0,1% de ácido trifluoroacético, 90% de agua, 10% de metanol;

Disolvente B: 0,1% de ácido trifluoroacético, 90% de metanol, 10% de agua;

Procedimiento V:

Gradiente lineal de 0 a 100% B durante 1,5 min, con 1,7 min a 100% B;

Sistemas de la serie Agilent 1200 acoplados con DADetector usando Agilent chemstation y usando software Chemstation B.04.01 (482); con fuente de ionización ESI tanto en modo positivo como negativo.

Visualización UV a 220 nm;

Columna: Waters Xbridge Phenyl 4,6 x 30 mm 3.5 um

Programa de Gradiente: Tiempo (min)/%B: 0/0,1.5/100,3.2/100,3.6/0,4.0/0

Caudal: 1,8 ml/min;

Tampón: Formiato amónico 10 mM en agua.

Fase móvil A: Tampón: Acetonitrilo: 98:02

Fase móvil B: Tampón: Acetonitrilo: 02:98

Procedimiento W:

Gradiente lineal de 0 a 100% B durante 2,50 min, con 0,5 min tiempo de retención a 100% B;

Sistemas de la serie Agilent 1200 acoplados con DADetector usando Agilent chemstation y usando software Chemstation B.04.01 (482) con fuente de ionización en multimodo, tanto en modo positivo como negativo.

Visualización UV a 220 nm;

Columna: Merck Puroshpere @ Star RP-18 4 x 5 mm, 3u

Programa de Gradiente: Tiempo (min)/%B: 0/0,2.0/100,2.5/100,3.0/0,3.5/0

Caudal: 2,5ml/min;

Tampón: acetato amónico 20mM en agua.

Fase móvil A: Tampón: Acetonitrilo: 90:10

Fase móvil B: Tampón: Acetonitrilo: 10:90

Procedimiento X:

Gradiente lineal de 0 a 100% de B durante 2 min;

Visualización UV a 220 nm;

Columna: Phenomenex Luna C18 4,6 x 30 mm;

Caudal: 5 ml/min;

Disolvente A: Acetato amónico 10 mM, 90% de agua, 10% de metanol-,

Disolvente B: Acetato amónico 10 mM, 90% de metanol, 10% de agua.

Procedimiento Y:

La HPLC/EM analítica de fase inversa se realizó en sistemas de la serie Agilent 1200 acoplado con DADetector, espectrómetro de masas Ion-Trap 6330, 1200 ELSD (Agilent) usando software Agilent chemstation & Brooker 4.0 Build 234 en modo tanto positivo como negativo.

Gradiente lineal de 0 a 100% B durante 1,2 min, con 1,8 min tiempo de retención a 100% B;

Sistemas de la serie Agilent 1200 acoplados con DADetector

Visualización UV a 220 nm;

Columna: Ascentis Express C18 2,1 x 50 mm, 2,7u

Programa de Gradiente: Tiempo (min)/%B: 0/0,1.2/100,3.0/100,3.4/0,4.0/0

Caudal: 1,0ml/min;

Tampón: Formiato amónico 10 mM en agua.

Fase móvil A: Tampón: Acetonitrilo: 98:02

Fase móvil B: Tampón: Acetonitrilo: 02:98

Procedimiento Z:

La HPLC/EM analítica de fase inversa se realizó en sistemas de la serie Agilent 1200 acoplado con DADetector, espectrómetro de masas Ion-Trap 6330, 1200 ELSD (Agilent) usando software Agilent chemstation & Brooker 4.0 Build 234 en modo tanto positivo como negativo.

Gradiente lineal de 0 a 100% B durante 1,2 min, con 1,8 min tiempo de retención a 100% B;

Sistemas de la serie Agilent 1200 acoplados con DADetector

Visualización UV a 220 nm;

Columna: Zorbax AQ C18 4,6 x 50 mm, 3,5u

Programa de Gradiente: Tiempo (min)/%B: 0/2,1.5/20,4.0/95,4.5/2,6/2

Caudal: 1,0ml/min;

Tampón: 0,1% de ácido fórmico en agua.

Fase móvil A: 0,1% de ácido fórmico en agua.

Fase móvil B: acetonitrilo.

Procedimiento Z1:

Información del procedimiento:

A: Water:ACN (95:5); acetato amónico 10mM

B: Water:ACN (5:95); acetato amónico 10mM

Caudal: 4 ml/min

Temp: 45°C

Columna: Ascentis Express C18 (50 x 4,6), 2,7µm

Tiempo (min): 0---4

Procedimiento A1:

Gradiente lineal de 10 a 100% B durante 12 min, con 3 min TIEMPO DE RETENCIÓN a 100% B;

Programa de Gradiente: T/%B: 0/10, 12/100, 15/100, 18/10, 23/10

Visualización UV a 220 y 254 nm;

Waters Sunfire C18 (4,6 x 150 mm, 3,5u)

Caudal: 1 ml/min

Tampón: 0,05% de ácido trifluoroacético en agua, a pH ajustado a 2,5 con amoniaco dil.

Fase móvil A: Tampón: Acetonitrilo: 95:05

Fase móvil B: Tampón: Acetonitrilo: 05:95

Procedimiento A2:

Gradiente lineal de 10 a 100% B durante 12 min, con 3 min TIEMPO DE RETENCIÓN a 100% B;

Programa de Gradiente: T/%B: 0/10, 12/100, 15/100, 18/10, 23/10

Visualización UV a 220 y 254 nm;

Waters Xbridge Phenyl (4,6 x 150 mm, 3,5u)

Caudal: 1 ml/min

Tampón: 0,05% de ácido trifluoroacético en agua, a pH ajustado a 2,5 con amoniaco dil.

Fase móvil A: Tampón: Acetonitrilo: 95:05

Fase móvil B: Tampón: Acetonitrilo: 05:95

Procedimiento A3:

Gradiente lineal de 10 a 100% B durante 12 min, con 8 min TIEMPO DE RETENCIÓN a 100% B;

Programa de Gradiente: Tiempo (min)/%B: 0/10, 12/100, 20/100, 23/10, 26/10

Visualización UV a 220 y 254 nm;

Waters Xbridge Phenyl (4,6 x 150 mm, 3,5u)

Caudal: 1,0 ml/min;

Fase móvil A: Bicarbonato amónico 10 mM en agua, a pH ajustado a 9,5 con amoniaco dil.

Fase móvil B: Metanol

Procedimiento A4:

Gradiente lineal de 0 a 100% B durante 10 min, con 5 min a 100% B;

Visualización UV a 220 nm;

Columna: X-bridge fenilo 4,6 x 150 mm;

Caudal: 1 ml/min;

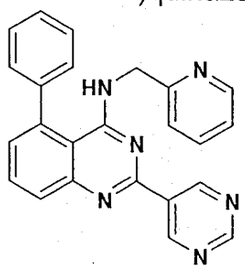
Disolvente A: 0,1% de ácido trifluoroacético, 90% de agua, 10% de acetonitrilo;

Disolvente B: 0,1% de ácido trifluoroacético, 90% de acetonitrilo, 10% de agua;

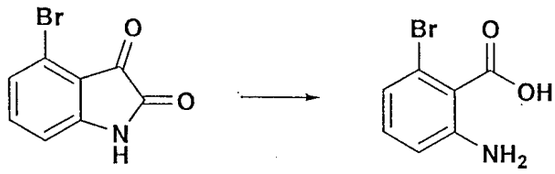
Los espectros de RMN ^{1}H se obtuvieron con espectrómetros de transformada JEOL FOURIER® que funcionan a las frecuencias siguientes: RMN ^{1}H: 400 MHz (Bruker o JEOL) o 500MHz (JEOL). RMN ^{13}C: 100 MHz (Bruker o JEOL). Los datos de espectros se exponen en el formato: desplazamiento químico (multiplicidad, constantes de acoplamiento y número de hidrógenos). Los desplazamientos químicos se especifican en ppm a campo bajo de un patrón interno de tetrametilsilano (unidades δ, tetrametilsilano= 0 ppm) y/o en referencia a los picos de disolvente, que en el espectro de RMN ^{1}H aparecen a 2,49 ppm para CD_2HSOCD_3, 3,30 ppm para CD_2HOD y 7,24 ppm para $CHCl_3$, y que en el espectro de RMN ^{13}C aparecen a 39,7 ppm para CD_3SOCD_3, 49,0 ppm para CD_3OD y 77,0 ppm para $CDCl_3$. Todos han sido espectros de RMN ^{13}C desacoplados de protones.

EJEMPLO 1

5-fenil-N-(piridin-2-ilmetil)-2-(pirimidin-5-il)quinazolin-4-amina

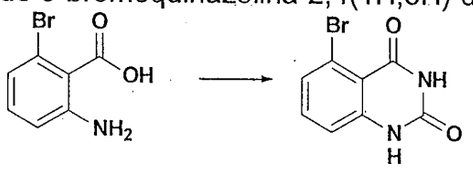


Etapa 1. Preparación de ácido 2-amino-6-bromobenzoico



A 4-bromoindolin-2,3-diona (8,94 g, 39,6 mmol) se añadió hidróxido sódico 1,0M (40 ml, 120 mmol) dando una mezcla marrón oscuro. La mezcla se calentó hasta 80ºC, después, lentamente se añadió peróxido de hidrógeno al 20% (9 ml, 88 mmol) durante 15 min (precaución: tras la adición del reactivo se observó una fuerte reacción exotérmica). Después, la mezcla se agitó a 80ºC durante 1 hora. Después de este tiempo, la mezcla se enfrió en un baño de hielo hasta ~ 10ºC y, después, se concentró hasta obtener un residuo. Con precaución se añadió HCl hasta que el pH de la mezcla fue 4-5. Una vez con el pH prescrito, la mezcla se concentró después hasta sequedad y se añadió MeOH (150 ml). La suspensión resultante se agitó durante 15 min y después se filtró. El filtrado se concentró hasta sequedad y se secó al vacío durante 14 horas, dando ácido 2-amino-6-bromobenzoico (9,18 g) en forma de un sólido marrón. RMN ^{1}H (400 MHz, DMSO-d_6) δ ppm 6,72 (1 H, t, *J*= 7,91 Hz), 6,60 (1 H, dd, *J*= 7,78, 1,00 Hz), 6,52 (1 H, dd, *J*= 7,91, 1,13 Hz). CLEM (Procedimiento D): tiempo de retención 0,68 min [M+1] 200.0.

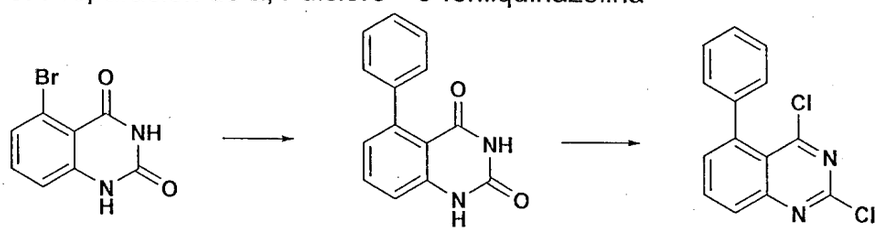
Etapa 2. Preparación de 5-bromoquinazolina-2,4(1H,3H)-diona



El ácido 2-amino-6-bromobenzoico (2,97 g, 13,7 mmol) se suspendió en una mezcla de agua (100 ml) y ácido acético (1,5 ml) a 35ºC, después, lentamente se añadió a la mezcla una suspensión de cianato sódico (2,23 g,

34,4 mmol) en 10 ml de agua. Tras la finalización de la adición, la mezcla resultante se agitó a 35ºC durante 30 minutos y, después, lentamente se añadieron a la mezcla pastillas de hidróxido sódico (24,7 g, 619 mmol) dando un precipitado espeso. La mezcla se enfrió hasta 5ºC en un baño de hielo y el pH de la suspensión se ajustó a 4 usando HCl concentrado. Una vez al pH prescrito, la suspensión se filtró y el sólido se lavó con agua y se secó al vacío al tiempo que se calentaba a 100ºC, dando 5-bromo-1H-quinazolina-2,4-diona (1,91 g) en forma de un sólido marrón. RMN ^{1}H (400 MHz, DMSO-d_6) δ ppm 11,30 (1 H, a, s,), 11,26 (1 H, a, s,), 7,43 - 7,48 (1 H, m), 7,40 (1 H, dd, *J*=7,78, 1,25 Hz), 7,16 (1 H, dd, *J*=7,91, 1,13 Hz).

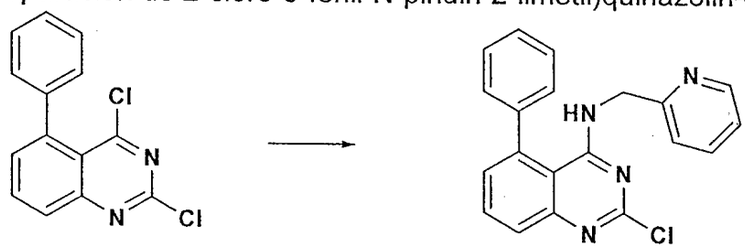
Etapa 3. Preparación de 2,4-dicloro—5-fenilquinazolina



Véase *J. Med. Chem.*, 50(7):1675 (2007), 76759-011. A una mezcla de 5-bromoquinazolina-2,4(1H,3H)-diona (900 mg, 3,73 mmol) y $Pd(Ph_3P)_4$ (216 mg, 0,187 mmol) en DME (90 ml) se añadió ácido fenilborónico (683 mg, 5,60 mmol), seguido por una solución de bicarbonato sódico (941 mg, 11,2 mmol) en agua (30 ml) y la reacción se calentó a reflujo durante 40 horas. Al final de este periodo se retiró el disolvente orgánico a presión reducida. La mezcla resultante se filtró y el sólido se lavó con agua. El sólido se concentró a presión reducida en MeOH/DCM para eliminar el agua, dando 5-fenilquinazolina-2,4(1H,3H)-diona en forma de un sólido blancuzco. La 5-fenilquinazolina-

2,4(1H,3H)-diona (9,64 g, 40,4 mmol) se añadió a $POCl_3$ (75 ml, 810 mmol) seguido por $PhN(CH_3)_2$ (10,3 ml, 81,0 mmol). Tras la finalización de la adición, la mezcla de reacción se calentó hasta reflujo (105ºC), en el que se agitó durante 2 horas. Después de este tiempo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente. Una vez a la temperatura prescrita, la mezcla de reacción se concentró a presión reducida, se diluyó con DCM y, después, se inactivó mediante la adición de solución de K_3PO_4 1M fría. Se separó la capa orgánica y la capa acuosa se extrajo dos veces con DCM. Las capas orgánicas combinadas se secaron sobre $MgSO_4$, se filtraron y se concentraron a presión reducida, dando un residuo. El residuo se purificó mediante cromatografía ISCO (columna de 330 g) usando hexanos/EtOAc (0-25% durante 20 min, caudal 100 ml/min) dando 2,4-dicloro-5-fenilquinazolina (7,11 g, rendimiento 63,9%) en forma de un sólido amarillo. RMN ^1H (400 MHz, cloroformo-d) ppm 8,04 (1 H, m) 7,96 (1 H, m) 7,59 (1 H, dd, *J*= 7,28, 1,25 Hz) 7,45 (3 H, dd, *J*= 5,02, 1,76 Hz) 7,32 (2 H, m).

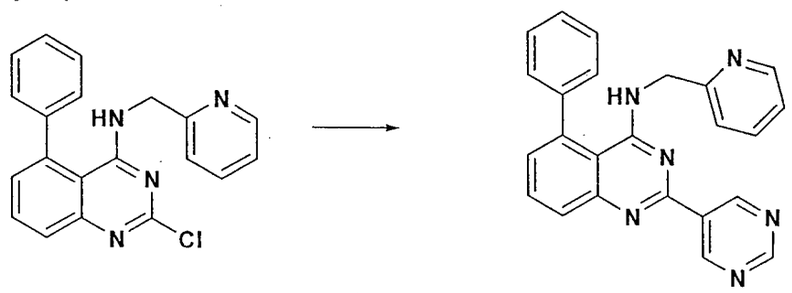
Etapa 4. Preparación de 2-cloro-5-fenil-N-piridin-2-ilmetil)quinazolin-4-amina



El compuesto 2,4-dicloro-5-fenilquinazolina (1,38 g, 5,03 mmol) se disolvió en THF (80 ml) y gota a gota se añadió trietilamina (1,33 ml, 9,56 mmol). La mezcla se agitó durante 5 min a temperatura ambiente y, después, gota a gota se añadió piridin-2-ilmetanamina (0,57 ml, 5,53 mmol). La mezcla

resultante se agitó a temperatura ambiente durante 14 horas. En este momento, la mezcla se filtró a través de una frita de vidrio de porosidad media, se concentró hasta sequedad a presión reducida y, después, se purificó mediante cromatografía en columna ISCO ultrarrápida (columna en gel de sílice de 80 g) eluyendo con 0-100% de acetato de etilo/hexanos durante 30 minutos proporcionando 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (1,32 g, 75%). CLEM Procedimiento A [M+1] se observó 347,1. Procedimiento B HPLC: Pureza 99,1% Tiempo de retención 6,66 min. RMN ^{1}H (400 MHz, cloroformo-d) δ ppm 8,16 (1 H, d, *J*= 4,77 Hz), 7,79 (1 H, d, *J*= 7,28 Hz), 7,70 (1 H, t, *J*= 7,78 Hz), 7,59 (1 H, dt, *J*= 7,53, 1,51 Hz), 7,40 - 7,55 (5 H, m), 7,08 - 7,25 (4 H, m), 4,66 (2 H, d, *J*= 4,02 Hz).

Etapa 5. Ejemplo 1

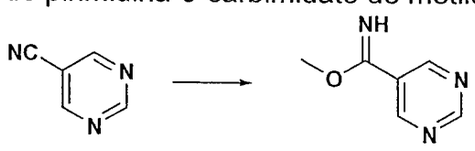


Los compuestos 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (225 mg, 0,649 mmol), ácido pirimidin-5-ilborónico (121 mg, 0,973 mmol) y cloruro de bis(trifenilfosfina)paladio (II) (23 mg, 0,032 mmol) se combinaron en un tubo microondas que se selló, evacuó y, después, se rellenó con argón. En argón, a la mezcla de reacción se añadieron dioxano (1 ml) previamente desgasificado) y una solución de carbonato de sodio (0,33 ml, 0,330 mmol) en agua (0,33 ml). La mezcla resultante se calentó bajo radiación con microondas

hasta 100ºC, en la que se mantuvo durante 60 minutos. Después de este tiempo se añadieron ácido pirimidin-5-il-borónico (91 mg, 0,7773 mmol) y cloruro de bis(trifenilfosfina)paladio (II) (17 mg, 0,024 mmol) adicionales. Tras la finalización de la adición, la mezcla resultante se calentó con radiación de microondas a 100ºC durante 40 minutos y, después, se dejó enfriar hasta la temperatura ambiente, a la que se agitó durante 14 minutos. Al final de este periodo, la mezcla de reacción se diluyó con 50 ml de cada uno de agua y acetato de etilo. Se separó las capas y la porción acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con 50 ml de salmuera, se secaron sobre Na_2SO_4, se decantaron y se concentraron a presión reducida, dando un residuo crudo. El residuo crudo se purificó mediante ISCO (columna en 40 g de gel de sílice) eluyendo con 0-5% de MeOH durante 15 minutos y, después, con 5% de MeOH durante 10 minutos, dando el Ejemplo 1 (212 mg, 84%). RMN ^{1}H (400 MHz, $CDCl_3$) ppm 4,74 (d, *J*= 4,27 Hz, 2 H) 6,73 - 6,81 (m, 1 H) 7,09 - 7,16 (m, 2 H) 7,25 - 7,29 (m, 1 H) 7,44 - 7,52 (m, 5 H) 7,58 (dt, *J*= 7,72, 1,88 Hz, 1 H) 7,73 (dd, *J*= 8,28, 7,28 Hz, 1 H) 7,93 (dd, *J*= 8,28, 1,25 Hz, 1 H) 8,23 - 8,26 (m, 1 H) 9,29 (s, 1 H) 9,78 (s, 2 H). CLEM Procedimiento D: tiempo de retención 0,76 min, [M+1] = 391; HPLC Procedimiento B: pureza 99%, tiempo de retención 5,6 min.

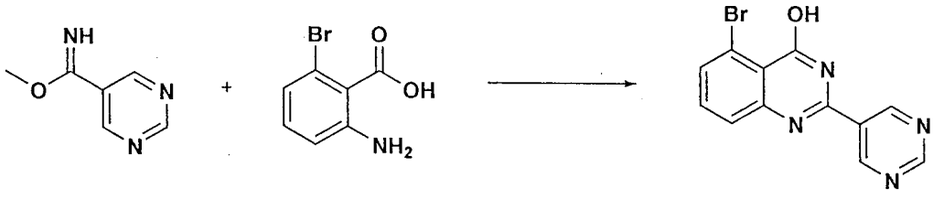
Como alternativa, el Ejemplo 1 se puede sintetizar del siguiente modo:

Etapa 1. Preparación de pirimidina-5-carbimidato de metilo



A una suspensión agitada de 5-cianopirimidina (5,0 g, 47 mmol) en metanol (50 ml) se añadió 25% en peso de metóxido sódico en metanol (1,2 g, 23 mmol). La mezcla se agitó a temperatura ambiente durante 17 horas en atmósfera de nitrógeno y, después, gota a gota se añadió ácido acético (2,72 ml, 47 mmol). La mezcla resultante se agitó durante 4 horas y después se evaporó a presión reducida para eliminar el metanol y dar un residuo. El residuo se disolvió en éter (150 ml) y los sólidos se eliminaron mediante filtración. El filtrado se concentró a presión reducida dando pirimidina-5-carbimidato de metilo (4,9 g, rendimiento del 75%). Se usó el producto bruto sin purificación adicional. RMN ^{1}H (400 MHz, DMSO-d_6) δ: 3,83 (s, 3H); 9,18 (s, 2H); 9,30 (s, 1H); 9,54 (s, 1H). ES-EM: [M^++1] = 138.

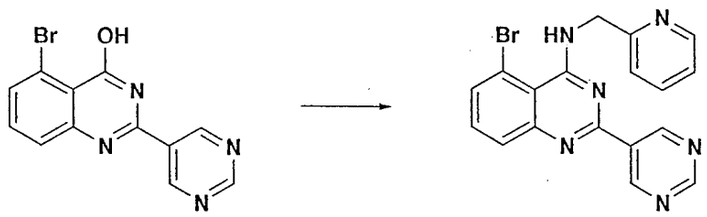
Etapa 2. Preparación de 5-bromo-2-(pirimidin-5-il)quinazolin-4-ol



A una suspensión agitada de pirimidina-5-carbimidato de metilo (2,00 g, 14,5 mmol) en metanol (20 ml) se añadió ácido 2-amino-6-bromobenzoico (3,1 g, 14,5 mmol). La mezcla se calentó hasta reflujo, durante el cual se agitó durante 16 horas en atmósfera de nitrógeno. Al final de este periodo, gota a gota se añadió ácido acético (2,73 ml, 47 mmol). Tras la finalización de la adición, el metanol se evaporó a presión reducida dando un residuo. El residuo se trituró con éter (100 ml), acetato de etilo (50 ml) y el sólido resultante se secó dando 5-bromo-2-(pirimidin-5-il)quinazolin-4-ol (1,2 g, 27%) en forma de un sólido blancuzco. Se usó el producto bruto sin purificación

adicional. RMN ^{1}H (400 MHz, DMSO-d_6) δ: 7,64 (dd, *J* = 7,2Hz, 8,4Hz, 1H); 7,73-7,75 (m, 2H); 9,35 (s, 1H); 9,46 (s, 2H); 12,9 (a s, 1H). ES-EM: [M^++1] = 303 y [M^++3] = 305.

Etapa 3. Preparación de 5-bromo-N-(piridin-2-ilmetil)-2-(pirimidin-5-il)quinazolin-4-amina

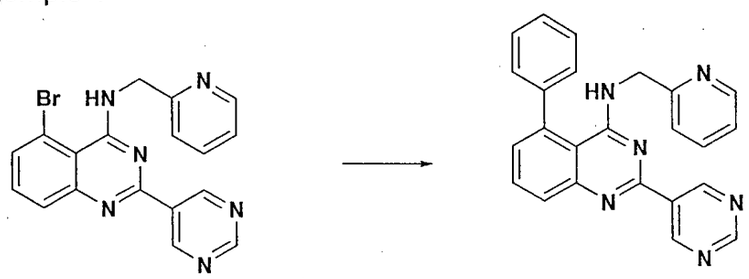


A una suspensión agitada de 5-bromo-2-(pirimidin-5-il)quinazolin-4-ol (2,0 g, 6,5 mmol) en DMF (20 ml) se añadió diisopropiletilamina (3,4 ml, 19 mmol), seguido por PyBroP (3,7 g, 7,9 mmol). Después de 5 min agitando a temperatura ambiente, a la reacción se añadió 2-aminometilpiridina (1,0 ml, 9,8 mmol). Tras la finalización de la adición, la mezcla de reacción se calentó hasta 80ºC, y a esa temperatura se agitó durante 2 horas (tiempo durante el cual la reacción se convirtió en una solución transparente). Al finalizar de este periodo, la mezcla de reacción se inactivó mediante la adición de agua fría y, después, se extrajo en una mezcla de acetato de etilo y hexano al 50% (200 ml). Los extractos orgánicos se secaron, se concentraron, se purificaron mediante cromatografía en columna usando acetato de etilo y hexanos como eluyente dando el producto bruto. El producto bruto se purificó adicionalmente mediante trituración con acetato de etilo y hexano, dando 5-bromo-N-(piridin-2-ilmetil)-2-(pirimidin-5-il)quinazolin-4-amina (0,5 g, rendimiento de 20%). RMN ^{1}H (400 MHz, $CDCl_3$) δ: 5,07 (d, *J* = 4,4Hz, 2H); 7,26 (m, 1H); 7,41 (d, *J* = 7,6

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Hz, 1H); 7,53 (t, *J* = 8 Hz, 1H); 7,71-7,73 (m, 2H); 7,86 (dd, *J* = 0,8 Hz, 8,4 Hz, 1H); 8,65 (d, *J* = 4 Hz, 1H); 9,30 (s, 1H); 9,38 (a s, 1H); 9,75 (s, 2H). ES-EM: $[M^+ +1]$ = 393 y $[M^+ +3]$ = 395.

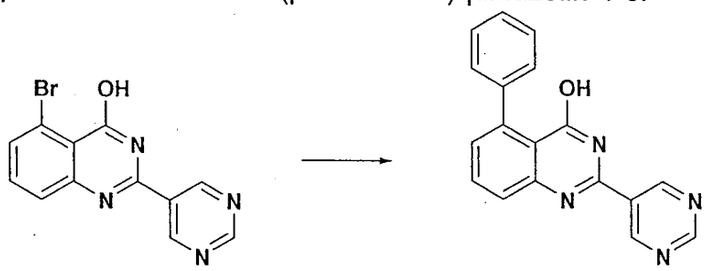
Etapa 4. Ejemplo 1



Una suspensión agitada de 5-bromo-N-piridin-2-ilmetil)-2-(pirimidin-5-il)quinazolin-4-amina (1,0 g, 2,5 mmol), ácido fenilborónico (0,46 g, 3,8 mmol) y carbonato de potasio (1,0 g, 7,6 mmol) en dimetoxietan—agua (3-1, 10 ml) se desgasificó y se cargó con tetraquistrifenilfosfeno de paladio (0,14 g, 0,12 mmol). Después, la mezcla se calentó hasta 90ºC, en la que se agitó durante 16 horas en atmósfera de nitrógeno. Tras este tiempo, la mezcla de reacción se inactivó con agua (5 ml) y a continuación se extrajo con acetato de etilo (3 x 25 ml). Los extractos orgánicos combinados se secaron y después se concentraron dando el producto bruto. El producto bruto se purificó mediante TLC preparativa usando cloroformo y metanol (95:5) como sistema disolvente dando el Ejemplo 1 (40 mg, rendimiento del 4%). RMN ^{1}H (400 MHz, DMSO-d_6) δ: 5,01 (d, *J* = 5,6 Hz, 2H); 7,27 (t, *J* = 4,0 Hz, 1H); 7,41-7,56 (m, 5H); 7,66-7,79 (m, 4H); 7,91 (d, *J* = 6,8 Hz, 1H); 8,42 (d, *J* = 8 Hz, 1H); 8,55 (d, *J* = 4,8 Hz, 1H); 9,23 (s, 1H); 9,32 (t, *J* = 6 Hz, 1H); 9,40 (s, 2H). CLEM Procedimiento O: tiempo de retención 1,67 min, [M+1] = 391. HPLC Procedimiento B: pureza 99%, tiempo de retención 8,5 min.

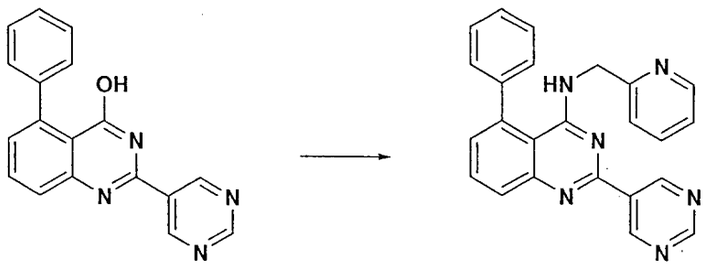
El Ejemplo 1 también se puede sintetizar del siguiente modo:

Etapa 1. Preparación de 5-fenil-2-(pirimidin-5-il)quinazolin-4-ol



Una suspensión agitada de 5-bromo-2-(pirimidin-5-il)quinazolin-4-ol (2,0 g, 6,6 mmol), ácido fenilborónico (1,2 g, 9,9 mmol) y una solución de carbonato de potasio (2,6 g, 19,8 mmol) en dimetoxietano y agua (3:1, 15 ml) se desgasificó y se cargó con dicloruro de 1,1'-bis(difenilfosfino)ferroceno de paladio (0,24 g, 0,33 mmol). La mezcla se calentó hasta 90ºC, en la que se agitó durante 24 horas en atmósfera de nitrógeno. Al final de este periodo, la mezcla de reacción se concentró dando el producto bruto. El producto bruto se purificó mediante cromatografía en columna ultrarrápida en gel de sílice usando 2% de metanol en diclorometano como eluyente, dando 5-fenil-2-(pirimidin-5-il)quinazolin-4-ol (800 mg, rendimiento del 27%). RMN ^{1}H (400 MHz, DMSO-d_6) δ: 7,29-7,40 (m, 6H); 7,79-7,87 (m, 4H); 9,37 (s, 1H); 9,45 (s, 2H); 12,59 (a s, 1H). CLEM Procedimiento O: tiempo de retención 1,68 min [M+1] 301.

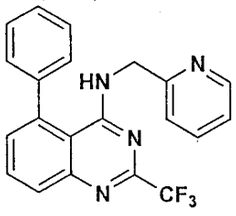
Etapa 2: Ejemplo 1



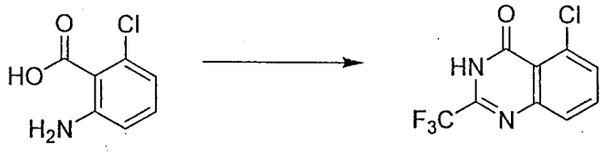
Posteriormente, el 5-fenil-2-(pirimidin-5-il)quinazolin-4-ol se convirtió en el Ejemplo 1 utilizando los reactivos y condiciones descritos para la preparación de 5-bromo-N-(piridin-2-ilmetil)-2-(pirimidin-5-il)quinazolina-4-amina en la etapa 3 en lo que antecede.

EJEMPLO 2

5-fenil-N-(piridin-2-ilmetil)-2-(trifluorometil)quinazolin-4-amina



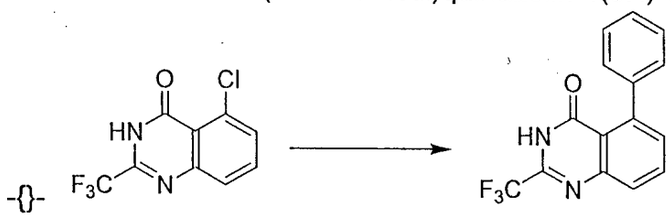
Etapa 1. Preparación de 5-cloro-2-(trifluorometil)quinazolin-4(3H)-ona



Véase la patente de EE.UU. nº 3.843.791. A una solución de ácido 2-amino-clorobenzoico (1,91 g, 11,13 mmol) en una mezcla de cloroformo (22 ml) y piridina seca (1,5 ml) a 0ºC se añadió anhídrido trifluoroacético (3,52 ml, 24,94 mmol). Tras la finalización de la adición, la mezcla de reacción se calentó hasta reflujo, en el que se agitó durante 2 horas. Después de este

tiempo, la mezcla de reacción se enfrió hasta la temperatura ambiente y se concentró, dando un material bruto. El material bruto se disolvió en cloroformo (22 ml), se saturó con gas amoniaco y después se agitó durante 30 minutos a temperatura ambiente. Después de este tiempo, la mezcla se concentró y el sólido resultante se lavó con HCl 1N (2 x 20 ml) y se diluyó con acetato de etilo (100 ml) y agua (100 ml). Se separó la capa orgánica y la capa acuosa se extrajo con acetato de etilo (10 ml). La capa orgánica se secó sobre $MgSO_4$, se filtró y se concentró, dando el producto bruto. El producto bruto se purificó mediante cromatografía ultrarrápida en gel de sílice eluyendo con 2-15% de acetato de etilo/hexanos dando 5-cloro-2-(trifluorometil)quinazolin-4(3H)-ona (1,3 g, 46%) en forma de un sólido blanco. RMN ^{1}H (400 MHz, cloroformo-d) ppm 10,23 (1 H, a. s.), 7,71 – 7,82 (2 H, m), 7,64 (1 H, d, *J*= 7,15 Hz). LCME Procedimiento A: tiempo de retención 0,65 min [M+1] = 250.

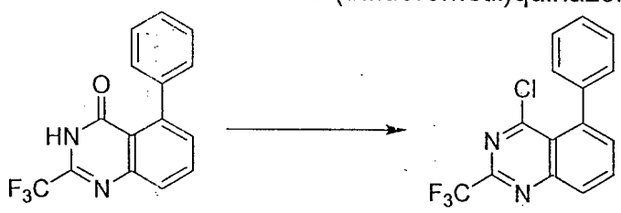
Etapa 2. Preparación de 5-fenil-2-(trifluorometil)quinazolin-4(3H)-ona



Los compuestos acetato de paladio (II) (19 mg, 0,085 mmol), fluoruro de potasio (498 mg, 8,57 mmol), 2-(di-terc-butilfosfino)bifenilo (51,1 mg, 0,171 mmol) y ácido fenilborónico (522 mg, 4,27 mmol) se combinaron en un vial de microondas en una atmósfera de argón. Se añadió una solución de 5-cloro-2-(trifluorometil)quinazolin-4(3H)-ona (710 mg, 2,86 mmol) en THF seco (9 ml) y la mezcla se calentó en el microondas a 100ºC durante 30 minutos. Después de este tiempo, la mezcla de reacción se diluyó con acetato de etilo (50 ml) y

se lavó con NaOH 1N (25 ml) y NaCl saturado (25 ml). La capa orgánica se separó, se secó sobre sulfato sódico y, después, se concentró a presión reducida dando el producto bruto (968 mg) que se usó en la siguiente etapa sin posterior purificación.

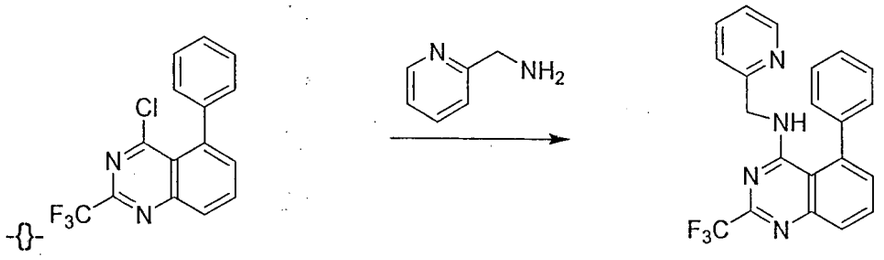
Etapa 3. Preparación de 4-cloro-5-fenil-2-(trifluorometil)quinazolina



Al material bruto de la Etapa 2, Ejemplo 3, se añadió oxicloruro fosforoso (2,86 ml, 307 mmol) y N,N-dimetilanilina (425 µl, 3,34 mmol). La mezcla de reacción se calentó hasta 100ºC, temperatura a la que se agitó durante 10 minutos. Después de este tiempo, la mezcla de reacción se enfrió hasta la temperatura ambiente. Una vez a la temperatura prescrita, los disolventes se retiraron a presión reducida dando un residuo, que después se disolvió en diclorometano (20 ml). La solución de diclorometano se añadió a 50 ml de una solución de KH_2PO_4 1,5M. Tras la finalización de la adición, el diclorometano se eliminó a presión reducida y la capa acuosa se extrajo con DCM (3 X 50 ml). Las porciones orgánicas combinadas se secaron sobre sulfato sódico y se concentraron a presión reducida, dando un segundo residuo. El segundo residuo se purificó mediante cromatografía ultrarrápida en gel de sílice eluyendo con 100% de DCM dando 4-cloro-5-fenil-2-(trifluorometil)quinazolina (612 mg, rendimiento del 59%) en forma de un sólido blanco. RMN ^{1}H (400 MHz, cloroformo-d) ppm 8,27 (1 H, d, *J*= 8,53 Hz), 8,07 (1 H, t, *J*= 7,78 Hz), 7,75 (1 H, d, *J*= 7,03 Hz), 7,42 - 7,54 (3 H, m), 7,29 - 7,38

(2 H, m). CLEM Procedimiento D: tiempo de retención 1,07 min [M+1] = 309.

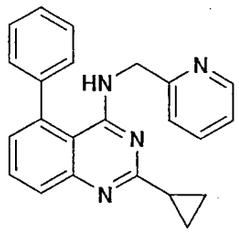
Etapa 4. Ejemplo 2

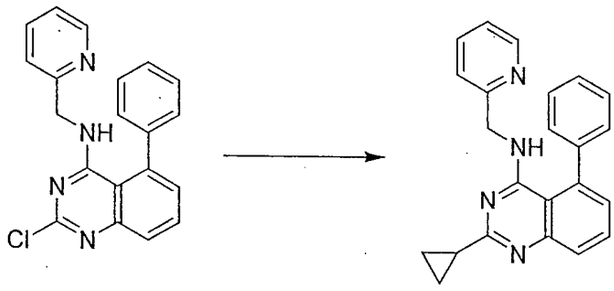


A una solución de 4-cloro-5-fenil-2-(trifluorometil)quinazolina (200 mg, 0,648 mmol) en THF (15 ml) se añadió trietilamina (0,172 ml, 1,231 mmol). Tras la finalización de la adición, la mezcla de reacción se agitó y se añadió piridin-1-ilmetanamina (0,080 ml, 0,777 mmol). La mezcla de reacción resultante se agitó a temperatura ambiente durante 1 hora y después se filtró. El filtrado se concentró a presión reducida dando un residuo. El residuo se purificó mediante cromatografía ultrarrápida en gel de sílice, eluyendo con 0-75% de acetato de etilo/hexanos, dando el Ejemplo 2 (217 mg, rendimiento del 88%) en forma de un sólido blanco. RMN ^{1}H (400 MHz, cloroformo-d) ppm 8,20 (1 H, d, *J*= 4,55 Hz), 7,99 (1 H, d, *J*= 8,34 Hz), 7,78 (1 H, t, *J*= 7,71 Hz), 7,59 (1 H, t, *J*= 7,58 Hz), 7,42 - 7,54 (5 H, m), 7,35 (1 H, d, *J*= 7,33 Hz), 7,03 - 7,22 (3 H, m), 4,69 (2 H, d, *J*= 4,04 Hz). CLEM Procedimiento D: tiempo de retención 0,90 min [M+1] = 381.

EJEMPLO 3

2-ciclopropil-5-fenil-N-(piridin-2-ilmetil)-quinazolin-4-amina



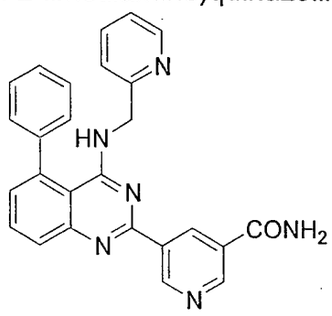


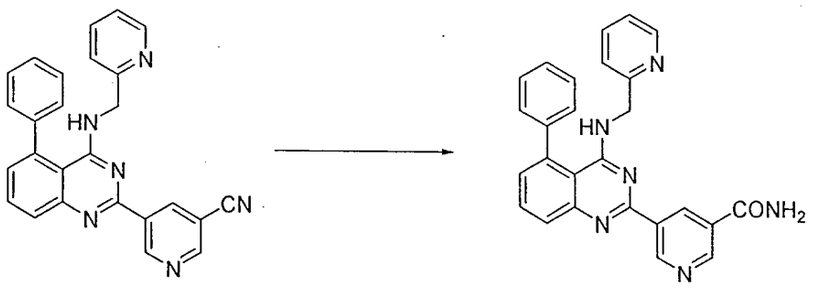
A una mezcla de bromuro de cinc (64,9 mg, 0,288 mmol) y complejo de dicloruro de 1,1'-bis(difenilfosfino)ferroceno-paladio (II) y diclorometano (5,89 mg, 7,21 µmol) se añadió THF anhidro (0,3 ml). Tras la finalización de la adición, la mezcla se enfrió hasta -78ºC. Una vez a la temperatura prescrita, gota a gota se añadió bromuro de ciclopropilmagnesio (0,288 ml, 0,144 mmol) y la mezcla se agitó a -78ºC durante 15 minutos. Al finalizar este periodo se añadió una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (50 mg, 0,144 mmol) en THF anhidro (1,5 ml). La mezcla resultante se agitó a -78ºc durante 1 hora y después se dejó calentar hasta la temperatura ambiente, a la que se agitó durante 18 horas. Después de este tiempo, la mezcla de reacción se diluyó con NH_4Cl saturado (5 ml) y la capa acuosa se extrajo con acetato de etilo (3 x 20 ml). Las porciones orgánicas se combinaron y se lavaron con NaCl saturado, se secaron sobre sulfato sódico y se concentraron a presión reducida, dando el producto bruto. El producto bruto se purificó mediante HPLC preparativa (YMC Sunfire 5u C18 30x100 mm, Fase móvil A:

10% de MeOH - 90% de H_2O – 0,1% de TFA, Fase móvil B: 90% de MeOH - 10% de H_2O – 0,1% de TFA, 20-100% de B durante 10 min, 100% B durante 2 min) dando el Ejemplo 3 (3,73 mg, rendimiento del 7%) en forma de un sólido amarillo claro. RMN ^1H (400 MHz, cloroformo-d) ppm 8,27 - 8,30 (1 H, m), 7,77 (1 H, dd, *J*= 8,46, 0,88 Hz), 7,63 (1 H, dd, *J*= 8,34, 7,07 Hz), 7,56 (1 H, td, *J*= 7,71, 1,77 Hz), 7,41 - 7,48 (5 H, m), 7,04 - 7,15 (3 H, m), 6,30 (1 H, a, s,), 4,57 (2 H, d, *J*= 4,55 Hz), 2,11 - 2,20 (1 H, m), 1,10 - 1,16 (2 H, m), 0,92 - 0,98 (2 H, m). CLEM Procedimiento D: tiempo de retención 0,76 min [M+1] = 353.

EJEMPLO 6

5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)nicotinamida





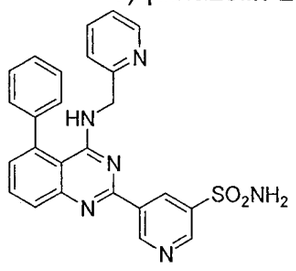
A una solución de 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)nicotinonitrilo (preparado de un modo similar a los procedimientos descritos en el Ejemplo 1, 200 mg, 0,48 mmol) en THF (5 ml) lentamente se añadió una

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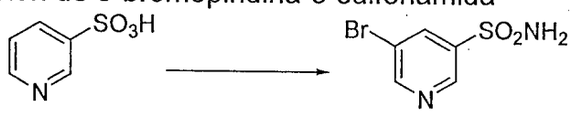
solución de hidróxido sódico (77 mg, 1,92 mmol) en H_2O (2 ml). La mezcla resultante se enfrió hasta 0ºC y se añadió 30% de % H_2O_2 (0,2 ml, 1,92 mmol). Tras la finalización de la adición, la mezcla de reacción se dejó calentar hasta la temperatura ambiente, a la que se agitó durante 16 horas. Al finalizar este periodo, la mezcla de reacción se filtró y purificó mediante TLC preparativa usando 5% de cloroformo en metanol, dando el Ejemplo 6 (50 mg) en forma de un sólido marrón. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,74 (d, *J* = 1,8 Hz, 1H), 9,18-9,15 (dd, *J* = 11,2, 1,6 Hz, 2H), 8,34 (s, 1H), 8,24 (d, *J* = 4,4 Hz, 1H), 7,95-7,93 (dd, *J* = 8,4, 1,2 Hz, 1H), 7,88-7,84 (dt, *J* = 7,2, 1,6 Hz, 1H), 7,76-7,71 (dt, *J* = 8,0, 1,6 Hz, 2H), 7,59-7,52 (m, 5H), 7,37-7,31 (dd, *J* = 13,6, 8,0 Hz, 2H), 7,24 (t, *J* = 6,0 Hz, 1H), 6,94 (t, *J* = 4,0 Hz, 1H), 4,78 (d, *J* = 4,0 Hz, 2H). CLEM Procedimiento O: tiempo de retención 1,39 min [M+1] = 433,0. Procedimiento B HPLC: pureza 97,9%, tiempo de retención 8,06 min.

EJEMPLO 7

5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-sulfonamida



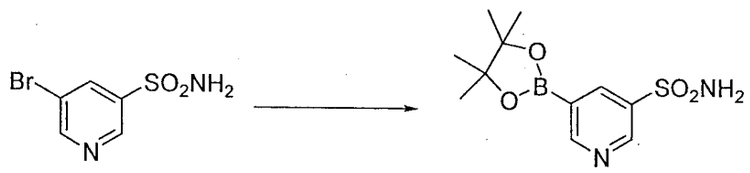
Etapa 1. Preparación de 5-bromopiridina-3-sulfonamida



Véanse también las publicaciones de EE.UU. nº 2006/217387 y

2006/375834, y *J. Org. Chem.*, 54:389 (1989). Una mezcla de ácido piridin-3-sulfónico (10,3 g, 64,8 mmol), pentacloruro de fósforo (20,82 g, 100 mmol) y oxicloruro de fósforo (10 ml, 109 mmol) se calentó hasta reflujo durante el que se agitó durante 4 horas. Al finalizar este periodo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente. Una vez a la temperatura prescrita, la mezcla de reacción se evaporó hasta sequedad a presión reducida, dando un residuo. El residuo se trató con bromo (6,00 ml, 116 mmol) y después se calentó hasta reflujo, al que se agitó durante 14 horas. Después de este tiempo, la mezcla de reacción se enfrió hasta 0°C y después, lentamente, se añadió una solución saturada de NH_4OH en H_2O (40 ml). La mezcla resultante se dejó calentar hasta la temperatura ambiente, momento en el que se agitó durante 30 minutos. Después, la mezcla de reacción se filtró y la torta de filtro se lavó con hexano dando 5-bromopiridin-3-sulfonamida (6,0 g) en forma de un sólido blancuzco. El producto se usó sin purificación adicional. CLEM Procedimiento Q: tiempo de retención 0,75 min [M+1] = 237,0.

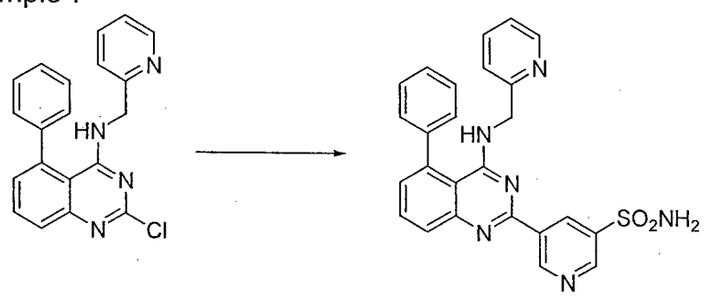
Etapa 2. Preparación de éster de pinacol de ácido piridin-3-sulfonamida-5-ilborónico



Véanse también los documentos WO2008/150827 A1 y WO2008/144463. Una mezcla de 5-bromopiridin-3-sulfonamida (1,5 g, 6,33 mmol), bis(pinacolato)diboro (2,41 g, 9,5 mmol) y acetato de potasio (1,86 g, 19,0 mmol) en 1,4-dioxano (15 ml) se desgasificó con nitrógeno durante 15

minutos, después se añadió el complejo cloruro de (1,1'-bis(difenilfosfino)-ferroceno)paladio (II) diclorometano (232 mg, 0,317 mmol) y la mezcla resultante se desgasificó de nuevo con nitrógeno durante 10 minutos. Al finalizar este periodo, la mezcla de reacción se calentó en un microondas a 120ºC durante 45 minutos. Después de este tiempo, la mezcla de reacción se filtró a través de CELITE® y el filtrado se concentró a presión reducida proporcionando éster de pinacol de ácido piridina-3-sulfonamida-5-ilborónico (740 mg) en forma de un sólido marrón. El producto se usó sin purificación adicional. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,83 (s, 1H), 8,80 (s, 1H), 8,26 (s, 1H), 7,56-7,74 (as, 2H), 1,17 (s, 12H).

Etapa 3. Ejemplo 7



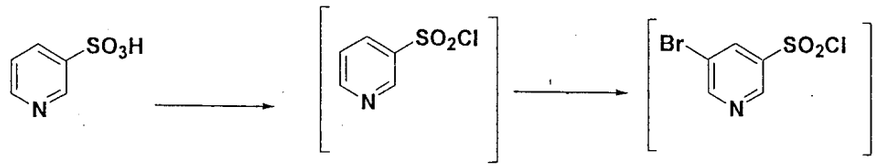
A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (150 mg, 0,43 mmol) en 1,4-dioxano (6 ml) y H_2O (1 ml) en nitrógeno se añadió éster de pinacol de ácido piridin-3-sulfonamida-5-ilborónico (185 mg, 0,65 mmol) y carbonato potásico (119 mg, 0,86 mmol). Tras la finalización de la adición, la mezcla se desgasificó con nitrógeno durante 15 minutos y, después, se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (31 mg, 0,043 mmol). La mezcla resultante se desgasificó de nuevo con nitrógeno durante 10 minutos. Tras este tiempo, la mezcla se

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calentó a 90ºC, temperatura a la cual se agitó durante 16 horas. Al finalizar este periodo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente. Una vez a la temperatura prescrita, la mezcla de reacción se inactivó mediante la adición de agua y después se transfirió a un embudo de separación. La capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El concentrado resultante se purificó mediante TLC preparativa usando 5% de metanol en diclorometano dando el ejemplo 7 (50 mg) en forma de un sólido marrón. RMN ^1H (400 MHz, DMSO-d_6) δ (ppm): 9,81 (s, 1H), 9,17 (s, 1H), 9,09 (s, 1H), 8,24 (d, *J* = 4,4 Hz, 1H), 7,94 (d, *J* =7,2 Hz, 1H), 7,86 (t, *J* = 7,6 Hz, 1H),7,75-7,72 (t, *J* = 7,6 Hz, 3H), 7,59-7,51 (m, 5H), 7,34 (d, *J* =7,2 Hz, 2H), 7,24 (t, *J* =6,4 Hz, 1H), 6,98 (t, *J* = 3,2 Hz, 1H), 4,77 (d, *J* = 4,0 Hz, 2H). CLEM Procedimiento Q: tiempo de retención 1,39 min [M+1] = 469,0. Procedimiento B HPLC: pureza 98,1%, tiempo de retención = 8,74 min.

Como alternativa, el Ejemplo 7 se puede sintetizar del siguiente modo:

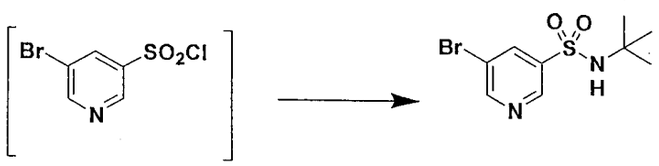
Etapa 1. Preparación de cloruro de 5-bromo-piridin-3-sulfonilo



Se añadieron los compuestos PCl_5 (2,95 Kg, 14,16 moles) ,y $POCl_3$

(2,45 Kg, 15,98 moles) en ácido piridin-3-sulfónico (1,5 kg, 9,42 mol) en un matraz RB de 10 l equipado con un agitador mecánico en atmósfera inerte. La masa de reacción se calentó hasta 120-125ºC, temperatura a la cual se agitó durante 18 horas. Tras este tiempo, la progresión de la reacción se siguió mediante HPLC, que indicó que la reacción había finalizado. El exceso de $POCl_3$ se retiró al vacío dando un residuo. El residuo se enfrió hasta la temperatura ambiente y se añadió bromo (1,2 kg, 7,5 moles). Tras la finalización de la adición, la mezcla resultante se calentó hasta 120-125ºC, temperatura a la que se agitó durante 5 horas. Al finalizar este periodo se siguió la progresión de la reacción mediante HPLC, que indicó que la reacción había finalizado. La mezcla de reacción se enfrió hasta la temperatura ambiente y después se vertió en agua helada (10 l) y la mezcla resultante se extrajo con DCM (10,5 l x 2). Los extractos de DCM se combinaron y el disolvente se eliminó al vacío dando el producto bruto (1,8 kg, rendimiento del 74,4,%).

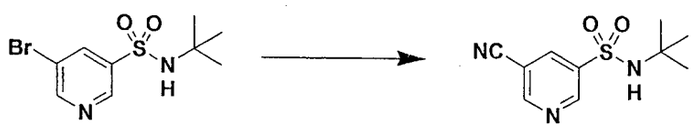
Etapa 2. Preparación de 5-bromo-N-terc-butilpiridin-3-sulfonamida



El cloruro de 5-bromopiridin-3-sulfonilo crudo de la etapa 1 anterior se disolvió en THF (14 l, 8 vol) y después se transfirió a un matraz RB de 20 l equipado con un agitador mecánica en atmósfera inerte. La solución se enfrió

hasta 0-5ºC y se añadió terc-butil-amina (1,95 kg, 26,66 moles) a 0-5ºC. Tras finalizar la adición, la mezcla de reacción se calentó hasta la temperatura ambiente, momento en el que se agitó durante 2 horas. Al finalizar este periodo, se siguió la progresión de la reacción mediante HPLC, que indicó que la reacción había finalizado. El disolvente se evaporó al vacío dando un residuo espeso. El residuo se disolvió en acetato de etilo (18 l, 12 vol.) La capa orgánica se separó, se lavó con agua (9 l, 5 vol.) y, después, se concentró al vacío dando un residuo. Se añadieron hexanos (9 l, 5 vol.) al residuo y el producto precipitó y se recogió mediante filtración, dando un sólido amarillo fluente (1,5 kg, rendimiento global del 54,28%). RMN ^{1}H (DMSO-D6, 400 MHz, δ ppm); 8,99 (d, *J* = 2Hz, 1H), 8,81 (d, *J* = 2 Hz, 1H), 8,29 (t, *J* = 2Hz, 1H). [M^{+}+1] = 293.

Etapa 3. Preparación de 5-bromo-N-terc-butilpiridin-3-sulfonamida



El compuesto 5-bromo-N-terc-butilpiridin-3-sulfonamida (1,5 kg, 5,11 moles) se disolvió en dimetilformamida (7,5 l, 5 vol.) y la solución se añadió a un reactor revestido de vidrio de 20 l equipado con un agitador mecánico. La solución se desgasificó con nitrógeno durante 30 minutos. Después de este tiempo, se añadieron ferrocianuro de potasio trihidrato (867 g, 2,05 moles), carbonato de sodio (1,08 kg, 10,189 moles), yoduro de cobre (I) (73,2 g, 0,374 moles) y dicloro-bis(trifenilfosfino) de paladio (II) (71,6 g, 0,102 moles). Tras la finalización de la adición, la mezcla de reacción se calentó hasta 120-125ºC,

temperatura a la que se agitó durante 4 horas. Al finalizar este periodo se siguió la progresión de la reacción mediante HPLC, que indicó que la reacción había finalizado. La mezcla de reacción se enfriará hasta la temperatura ambiente y después se filtró a través de un lecho de celite. Se añadió agua (18 l, 12 vol.) al filtrado y la mezcla resultante se extrajo con acetato de etilo (7,5 l x 2). Las capas orgánicas se combinaron, se lavaron con agua y después se concentraron dando un residuo espeso. Se añadieron hexanos (7,5 l, 5 vol.) al residuo. El producto se precipitó y se recogió mediante filtración, dando un sólido amarillo fluente (1,0 kg, rendimiento del 82,8%, pureza del 89% mediante HPLC). RMN ^{1}H (DMSO-D6, 400 MHz, δ ppm); 9,21 – 9,24 (d,d J= 7,2Hz, 3,2Hz, 2H), 8,70-8,71 (m,1H), 7,98 (s,1H). [M^++1] = 239,2.

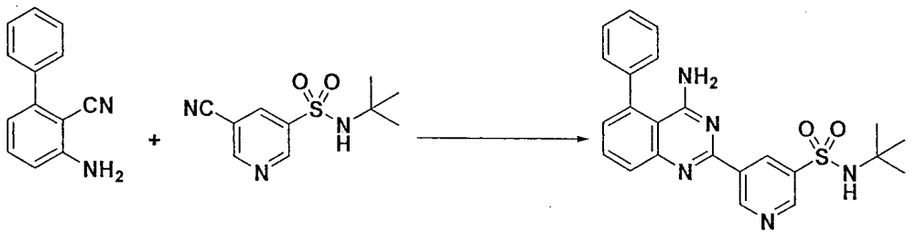
Etapa 4. Preparación de 3-aminofenil-2-carbonitrilo



A un reactor de 20 l equipado revestido de vidrio con un agitador mecánico se añadieron 2-amino-6-bromo-benzonitrilo (1,0 kg, 5,07 moles) y tolueno (10 l, 10 vol.) en atmósfera inerte. En la solución se añadieron acetato de potasio (996 g, 10,16 moles) y ácido fenilborónico (866, 7,10 moles) y la solución se desgasificó con nitrógeno durante 30 minutos. Después de este tiempo, a la mezcla de reacción se añadieron dicloro-bis(trifenilfosfino) de paladio (II) (17,8 g, 0,025 moles) a temperatura ambiente. La mezcla resultante se calentó hasta 110ºC, momento en el que se agitó durante 17

horas. Al finalizar este periodo se siguió la progresión de la reacción mediante HPLC, que indicó que la reacción había finalizado. La mezcla de reacción se filtró a través de un lecho de celite. El filtrado se transfirió de nuevo al reactor y se cargó ácido clorhídrico concentrado (~35%, 2 L, 2 vol.) en el reactor a temperatura ambiente. La sal de HCl del compuesto del título precipitó en la reacción y se recogió mediante filtración. La sal de HCl se transfirió al reactor de 20 l y después se basificó con una solución de NaOH al 10% (pH 8-9). El producto resultante se extrajo con acetato de etilo (10 l x 10 vol.). La capa de acetato de etilo se lavó con agua (5 l, 5 vol.) y, después, el disolvente se evaporó al vacío dando un residuo. Se añadieron hexanos (5 l, 5 vol.) al residuo a 35-40ºC y la suspensión espesa resultante se enfrió hasta la temperatura ambiente. Una vez a la temperatura prescrita, el producto se recogió mediante filtración proporcionando un sólido amarillo claro (802 g, 81,4%, 99% mediante HPLC). RMN ^{1}H (DMSO-D6, 400 MHz, δ ppm); 7,43-7,52 (m, 5H), 7,33-7,37 (m, 1H), 6,83 (d, *J*= 8Hz, 1H), 6,62 (d, *J*= 8Hz, 1H), 6,1 (s, 2H). ES-EM: [M^++1] = 194,23.

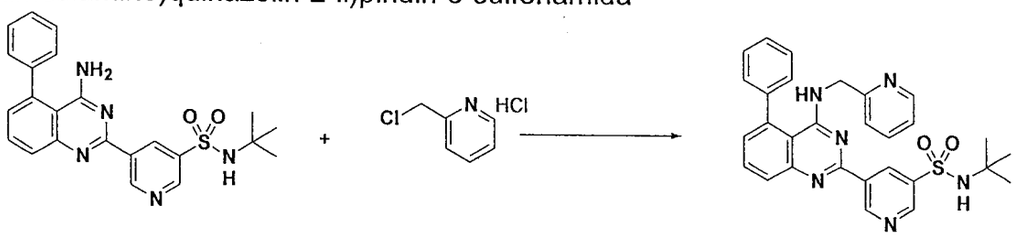
Etapa 5. Preparación de 5-(4-amino-5-fenilquinazolin-2-il)-N-terc-butilpiridin-3-sulfonamida



A un reactor de 20 l revestido con vidrio equipado con un agitador mecánico se añadieron 3-aminobifenil-2-carbonitrilo (1028 g, 5,30 moles), 5-

bromo-N-terc-butilpiridin-3-sulfonamida (1440 g, 5,55 moles) y 1,4-dioxano (10 l, 10 vol.). A la solución se añadió, en porciones, terc-butóxido de sodio (1,275 kg, 12,870 moles) a 20-30ºC. Tras finalizar la adición, la mezcla de reacción se calentó hasta reflujo, momento en el que se agitó durante 2 horas. Al finalizar este periodo, se siguió la progresión de la reacción mediante HPLC, que indicó que la reacción había finalizado. La mezcla de reacción se enfrió hasta 30-35ºC y después se vertió en agua (40 l, 40 vol.). La mezcla resultante se extrajo con DCM (20 l × 2). Las capas de DCM se combinaron, se lavaron con agua (10 l, 10 vol.) y, después, se secaron sobre sulfato sódico. El disolvente se evaporó al vacío dando un residuo. Al residuo se añadió alcohol isopropílico (1,2 l, 1,2 vol.) a 40ºC. La suspensión espesa precipitada resultante se enfrió hasta 10-15ºC y después se agitó durante 2 horas. Después de este tiempo, el precipitado se recogió mediante filtración y se secó a 50ºC durante 16 horas, dando el producto (1,9 Kg, rendimiento del 82,9%, pureza del 99% mediante HPLC). RMN ^{1}H (DMSO-D6, 400 MHz, δ ppm); 9,72 (s, 1H), 9,11 (s, 2H), 7,83-7,94 (m, 4H), 7,49-7,60 (m, 5H), 7,31 (d,d *J*= 6,8Hz ,1,2Hz, 1H). ES-EM: [M^++1] = 433,53.

Etapa 6. Preparación de N-terc-butil-5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-sulfonamida

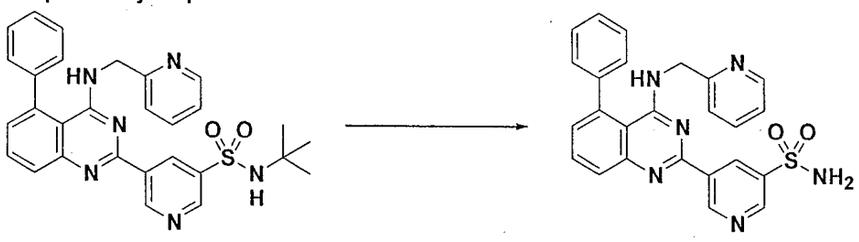


A un matraz RB de 20 l equipado con un agitador mecánico se

añadieron clorhidrato de 2-(clorometil)piridina (564 g, 3,44 moles) y acetamida de dimetilo (7 l, 7 vol.) en atmósfera inerte. La solución resultante se enfrió hasta 0-5ºC y se añadió trietilamina (346,3, 3,44 moles) a 0-5ºC. En un matraz 2 aparte RB de 20 l equipado con un agitador mecánico se añadieron 5-(4-amino-5-fenilquinazolin-2-il)-N-tec-butilpiridin-3-sulfonamida (1,0 kg, 2,306 moles) y dimetilacetamida (4 l, 4 vol.). Esta solución se enfrió hasta 0-5ºC y se añadió terc-butóxido de sodio (884 g, 9,24 moles) a 0-5ºC. La solución resultante se agitó para realizar la disolución y después se transfirió al matraz 1 RB a 0-5ºC. Tras la finalización de la adición, la mezcla de reacción se agitó a 0-5ºC durante 2 horas. Al finalizar este periodo, se siguió la progresión de la reacción mediante HPLC, que indicó que la reacción había finalizado. La masa de reacción se vertió en agua (60 l, 60 vol.) con agitación. El producto bruto se recogió mediante filtración y se secó a 60ºC durante 12 horas. Después de este tiempo, el material seco se disolvió en THF (20 l, 20 vol.). Tras la disolución, se añadió HCl 6M en alcohol isopropílico (1 l, 1 vol.) a 20-25ºC. La sal HCl bruta del producto se obtuvo en forma de un sólido amarillo claro fluente (920 g, rendimiento del 71%, pureza del 93% mediante HPLC). La sal HCl bruta (1,345 kg, 2,56 moles), metanol (6,7 l, 5 vol.) y diclorometano (13,5 l, 10 vol.) se añadieron a un reactor de 20 l revestido con vidrio equipado con un agitador mecánico. La suspensión espesa se agitó durante 20-30 min a 30ºC. Después de este tiempo, el disolvente se destiló hasta 4 vol. Con respecto a la entrada al vacío. La suspensión espesa resultante se enfrió hasta 20-25ºC, momento en el que se agitó durante 2 horas. Al finalizar este periodo, la suspensión espesa se filtró y se secó a 50ºC durante 6 horas dando el producto (1,1 kg, rendimiento del 82%, pureza del 98% mediante HPLC).

RMN ^{1}H (DMSO-D6, 400 MHz, δ ppm); 9,72 (s, 1H), 9,10-9,14 (m, 2H), 8,39 (s, 1H), 7,92-8,03 (m, 4H), 7,56-7,58 (m, 5H), 7,43-7,49 (m, 3H), 7,1 (as, 1H), 4,88 (s, 2H), 1,17 (2, 9H).

Etapa 7. Ejemplo 7



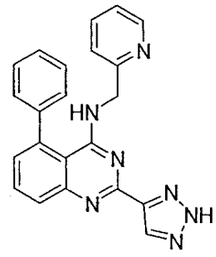
En un reactor de 20 l revestido con vidrio equipado con un agitador mecánico se añadieron N-terc-butil-5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-sulfonamida (1,0 kg, 1,9 moles) y ácido clorhídrico concentrado (7 l, 7 vol.). La mezcla resultante se calentó hasta 90-100ºC, momento en el que se agitó durante 1 hora. Al finalizar este periodo se siguió la progresión de la reacción mediante HPLC, que indicó que la reacción había finalizado. La mezcla de reacción se enfrió hasta 5-10ºC y el pH se ajustó hasta de 1,7 a 2,0 usando una solución de hidróxido sódico acuoso al 12%. Una vez al pH prescrito, la sal HCl bruta del producto se recogió mediante filtración. En un reactor de 10 l revestido con vidrio equipado con un agitador mecánico se añadieron la torta de filtro de la sal HCl y etanol (5 l, 5 vol.). La mezcla resultante se basificó hasta un pH 7-8 a 20-25ºC usando trietilamina (2,25 kg, 22,23 moles). Una vez al pH prescrito, la mezcla básica se agitó durante 2 horas. Después de este tiempo, la base libre del producto se filtró y se lavó con agua (10 l, 10 vol.) seguido por etanol (2 l, 2 vol.). El producto resultante se secó a 50-55ºC durante 8 horas dando el Ejemplo 7

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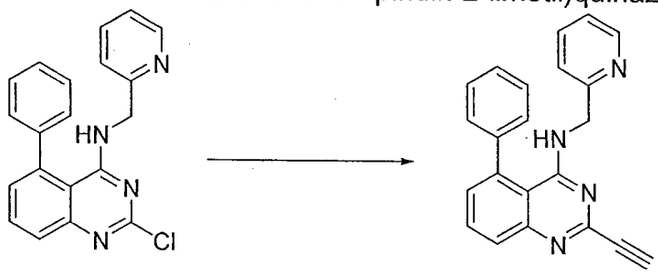
(644 g, rendimiento del 72%, pureza del 99,9% mediante HPLC). RMN ^{1}H (DMSO-D6, 400 MHz, δ ppm); 9,81 (d, *J*= 2,0Hz, 1H), 9,18 (t, J= 2 Hz, 1H), 9,11 (d, J= 2 Hz, 1H), 8,23 (d, J=4,4 Hz, 1H), 7,92-7,94 (m, 1H), 7,83-7,87 (m, 1H), 7,78 (s, 2H), 7,70-7,72 (m, 1H), 7,50-7,59 (m, 5H), 7,31-7,34 (m, 2H), 7,22-7,25 (m, 1H), 6,95 (t, J= 4 Hz, 1H), 4,76 (d, *J*= 4 Hz, 2H). ES-EM: [M^++1] = 469.

EJEMPLO 8

5-fenil-N-(piridin-2-ilmetil)-2-(2H-1,2,3-triazol-4-il)quinazolin-4-amina



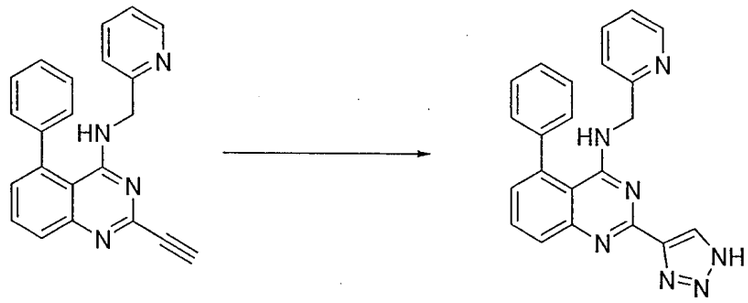
Etapa 1. Preparación de 2-etinil-5-fenil-N—piridin-2-ilmetil)quinazolin-4-amina



A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (1,0 g, 2,8 mmol) en DMF (10 ml) en nitrógeno se añadió trimetilsililacetileno (2,0 ml, 14 mmol), yoduro cúprico (0,11 g, 0,,58 mmol) y Et_3N (1,2 ml, 8,4 mmol). Tras la finalización de la adición, la mezcla se desgasificó con nitrógeno durante 15 minutos. después se añadió

tetraquis(trifenilfosfino)paladio (0,20 g, 0,28 mmol) y la mezcla resultante se desgasificó de nuevo con nitrógeno durante 10 minutos. Después de este tiempo, la mezcla de reacción se calentó en un tubo sellado hasta 120ºC, temperatura a la cual se agitó durante 16 horas. Al finalizar este periodo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente. Una vez a la temperatura prescrita, la mezcla de reacción se inactivó mediante la adición de agua. La mezcla de reacción resultante se extrajo con acetato de etilo y la capa orgánica se lavó sucesivamente con agua y salmuera. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El concentrado resultante se disolvió en metanol y se saturó con gas amonio. La solución saturada se agitó durante 2 horas a 0ºC y después se concentró a presión reducida, dando un residuo. El residuo se purificó mediante cromatografía en columna ultrarrápida usando acetato de etilo y éter de petróleo, dando 2-etinil-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (650 mg). RMN ^{1}H (400 MHz, $CDCl_3$) δ (ppm): 8,15 (d, *J* = 4,0 Hz, 1H), 7,86 (dd, *J* = 8,4, 1,2 Hz, 1H), 7,69 (t, *J* = 8,4 Hz, 1H), 7,56 (dt, *J* = 3,6, 1,6 Hz, 1H), 7,49-7,42 (m, 5H), 7,26-7,23 (m, 1H), 7,13-7,08 (m, 2H), 6,94 (as, 1H), 4,67 (d, *J* = 10,0 Hz, 2H), 3,02 (s, 1H). CLEM Procedimiento O: tiempo de retención 1,35 min [M+1] = 337,0.

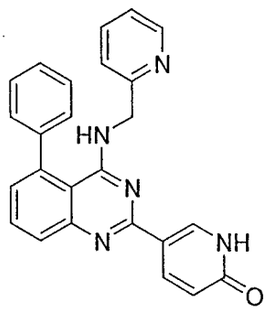
Etapa 2. Ejemplo 8



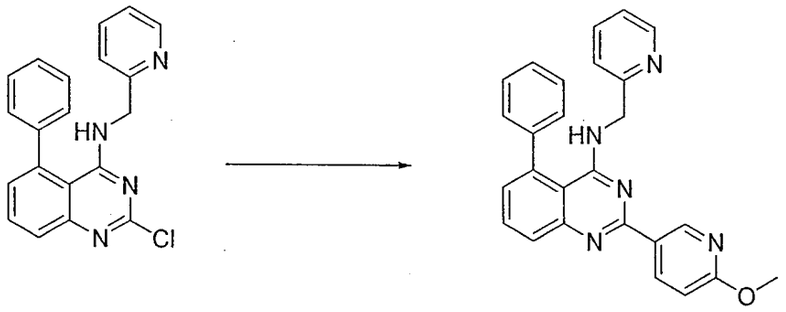
A una suspensión de 2-etinil-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,17g, 0,50 mmol) en tolueno (3 ml) se añadió trimetilsilazida (0,20 ml, 1,5 mmol). Tras la finalización de la adición, la mezcla de reacción se calentó en un tubo sellado hasta 120ºC, temperatura a la cual se mantuvo durante 2 días. Al finalizar este periodo, el tolueno se eliminó a presión reducida dando un residuo. El residuo se lavó con agua y después se extrajo con diclorometano. Los extractos orgánicos se secaron sobre Na_2SO_4, se filtraron y después se concentraron. El concentrado resultante se purificó mediante cromatografía en columna ultrarrápida en gel de sílice eluyendo con cloroformo y metanol (proporción 95:5), dando el Ejemplo 8 (90 mg) en forma de un sólido amarillo. RMN ^{1}H (400 MHz, CD_3OD) δ (ppm): 8,42 (as, 1H), 8,33 (d, *J* = 10,0 Hz, 1H), 7,92 (d, *J* = 10,0 Hz, 1H), 7,83 (t, *J* = 11,2 Hz, 1H), 7,76-7,72 (m, 2H), 7,49 (m, 5H), 7,31 (d, *J* = 10,8 Hz, 1H), 7,30-7,25 (m, 2H), 4,78 (s, 2H). CLEM Procedimiento O: tiempo de retención 1,36 min [M+1] = 380,2. Procedimiento B HPLC: pureza 98,5%, tiempo de retención 10,03 min.

EJEMPLO 10

5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-2(1H)-ona



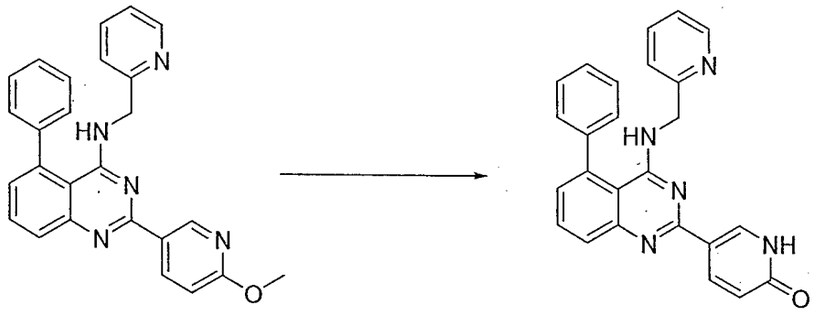
Etapa 1. Preparación de 2-(6-metoxipiridin-3-il)-5-fenil-N(piridin-2-ilmetil)-quinazolin-4-amina



A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (200 mg, 0,58 mmol) en DMF (10 ml) y H_2O (2 ml) en nitrógeno se añadió éster de pinacol de ácido 6-metoxipiridin-3-ilborónico (202 mg, 0,86 mmol) y carbonato potásico (160 mg, 1,16 mmol). Tras finalizar la adición, la mezcla se desgasificó con nitrógeno durante 15 minutos y después se añadió tetraquis(trifenilfosfina)paladio (66 mg, 0,0050 mmol). La mezcla resultante se desgasificó de nuevo con nitrógeno durante 10 minutos. Tras este tiempo, la mezcla de reacción se calentó a 90ºC, temperatura a la cual se agitó durante 12 horas. Después, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente y, después, se inactivó mediante la adición de agua. La mezcla de reacción se extrajo con acetato de etilo y la capa orgánica se lavó sucesivamente con agua y salmuera. Las capas orgánicas combinadas se

secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El concentrado resultante se purificó mediante cromatografía en columna ultrarrápida usando acetato de etilo al 16% en éter de petróleo, dando 2-(6-metoxipiridin-3-il)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (140 mg) en forma de un sólido marrón. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,26 (d, *J* = 2,4 Hz, 1H), 8,70-8,67 (dd, *J* = 8,8, 2,4 Hz, 1H), 8,23-8,22 (d, *J* = 5,2 Hz, 1H), 7,84-7,76 (m, 2H), 7,73-7,69 (dt, *J* = 8,0, 2,0 Hz, 1H), 7,58-7,48 (m, 5H), 7,32-7,30 (d, *J* = 7,6 Hz, 1H), 7,25-7,23 (m, 2H), 6,95-6,93 (d, *J* = 8,8 Hz, 1H), 6,81-6,79 (t, *J* = 4,0 Hz, 1H), 4,72-4,71 (d, *J* = 4,0 Hz, 2H), 3,94 (s, 3H). CLEM Procedimiento S: tiempo de retención 3,96 min [M+1] = 420,2. Procedimiento B HPLC: pureza 98,9%, tiempo de retención 8,93 min.

Etapa 2. Ejemplo 10

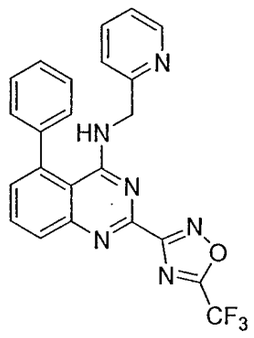


A una solución de 2-(6-metoxipiridin-3-il)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (140 mg, 0,33 mmol) en CH_2Cl_2 (2 ml) se añadió lentamente BBr_3 (416 mg, 1,66 mmol) a 0 °C. La mezcla de reacción se agitó a temperatura ambiente durante 72 horas antes de inactivar mediante la adición de solución acuosa de hidróxido amónico. Después, la mezcla de reacción se extrajo con CH_2Cl_2. La capa orgánica se lavó sucesivamente con agua y salmuera. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, se

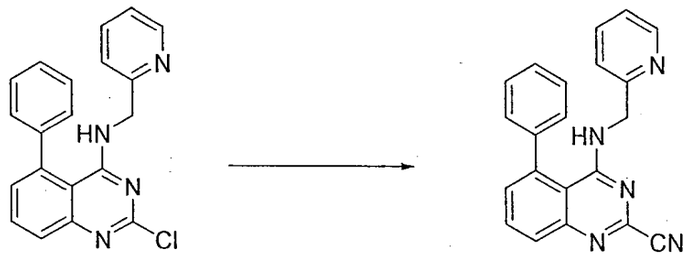
filtraron y se concentraron a presión reducida. El concentrado resultante se purificó mediante HPLC preparativa, dando el Ejemplo 10 (75 mg) en forma de un sólido blancuzco. Condiciones de la HPLC preparativa: Columna: Sunfire C18 (250 x 19 mm), Fase móvil A: 0,1% de TFA en H_2O, Fase móvil B: CH_3CN, Gradiente: 0 a 40% B durante 25 min, 100% B durante 10 min., Caudal: 14 ml/min, tiempo de retención: 20,5 min. RMN ^1H (400 MHz, DMSO-d_6) δ (ppm):8,68 (s, 1H), 8,41-8,38 (dd, *J* = 9,6, 2,8 Hz, 1H), 8,23 (d, *J* = 4,4 Hz, 1H), 8,09-7,94 (m, 3H), 7,84-7,79 (dt, *J* = 7,6, 1,6 Hz, 1H), 7,65-7,54 (m, 5H), 7,50-7,48 (d, *J* = 7,2 Hz, 1H), 7,40-7,38 (d, *J* = 8,0 HZ, 1H), 7,33-7,30 (t, *J* = 6,8 Hz, 1H), 6,62-6,60 (d, *J* = 9,6 Hz, 1H), 4,88 (d, *J* = 4,0 Hz, 2H). CLEM Procedimiento O: tiempo de retención 1,35 min [M+1] = 406,2. Procedimiento B HPLC: pureza 99,2%, tiempo de retención 10,26 min.

EJEMPLO 11

5-fenil-N-(piridin-2-ilmetil)-2-(5-trifluorometil)-1,2,4-oxadiazol-3-il)quinazolin-4-amina



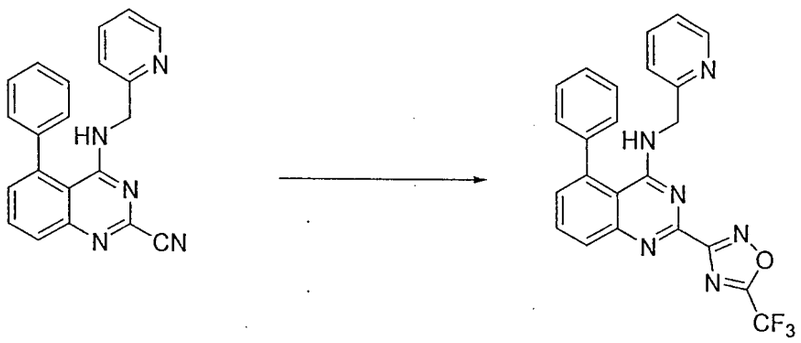
Etapa 1. Preparación de 5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-carbonitrilo



A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (5,0 g, 14 mmol) en CH_3CN (50 ml) se añadió cianuro de tetrametilamonio (4,5 g, 29 mmol), seguido por DBU (4,39 g, 28,88 mmol). Tras la finalización de la adición, la mezcla de reacción se calentó hasta 80ºC, temperatura a la que se agitó durante 12 horas. Después de este tiempo, la mezcla de reacción se inactivó con agua y después se extrajo con acetato de etilo. La capa orgánica se lavó sucesivamente con agua y salmuera, y las capas orgánicas combinadas se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El concentrado resultante se purificó mediante cromatografía en columna ultrarrápida usando acetato de etilo al 28% en éter de petróleo, dando 5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-carbonitrilo (2,1 g) en forma de un sólido marrón. RMN ^1H (400 MHz, DMSO-d_6) δ (ppm): 8,15-8,14 (d, J = 4,0 Hz, 1H), 7,96-7,87 (m, 2H), 7,75-7,70 (dt, J = 7,6, 2,0 Hz, 1H), 7,62-7,45 (m, 6H), 7,34-7,29 (m, 2H), 7,25-7,22 (m, 1H), 4,60 (d, J = 3,6 Hz, 2H). CLEM Procedimiento O: tiempo de retención 1,52 min [M+1] = 338,2.

Etapa 2. Ejemplo 11

000815

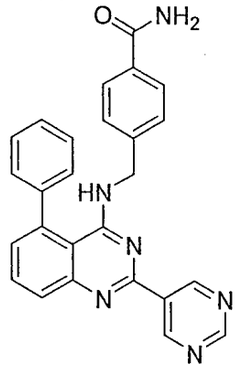


A una solución de 5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-carbonitrilo (150 mg, 0,45 mmol) en EtOH (5 ml) se añadió NH_2OH-HCl (62 mg, 0,90 mmol) seguido por Et_3N (125 µl, 0,90 mmol). La mezcla de reacción se calentó hasta reflujo, momento en el que se agitó durante 4 horas. Después de este tiempo, la mezcla de reacción se concentró a presión reducida dando un residuo. El residuo se disolvió en THF (5 ml). La solución resultante se enfrió hasta 0ºC y se añadieron piridina (145 µL, 1,80 mmol) seguida de anhídrido trifluoroacético (125 µl, 0,90 mmol). Tras la finalización de la adición, la mezcla de reacción se calentó hasta la temperatura ambiente, a la que se agitó durante 16 horas. Al finalizar este periodo, la mezcla de reacción se concentró a presión reducida dando un residuo. El residuo se purificó mediante cromatografía en columna ultrarrápida usando acetato de etilo 36% en éter de petróleo, dando el Ejemplo 11 (65 mg) en forma de un sólido blancuzco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,19 (d, *J* = 4,0 Hz, 1H), 7,99-7,91 (m, 2H), 7,75-7,71 (t, *J* = 7,2 Hz, 1H), 7,60-7,54 (m, 5H), 7,44 (d, *J* = 6,4 Hz, 1H), 7,36 (d, *J* = 7,6 Hz, 1H), 7,26-7,23 (m, 1H), 7,19 (m, 1H), 4,68-4,67 (d, *J* = 3,6 Hz, 1H). CLEM Procedimiento O: tiempo de retención 1,71 min [M+1] = 449,0. Procedimiento B HPLC: pureza 99,5%, tiempo de retención 9,66 min.

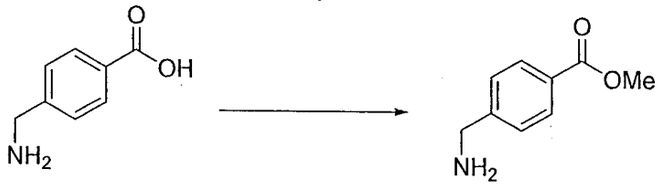
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EJEMPLO 12

4-((5-fenil-2-(pirimidin-5-il)quinazolin-4-ilamino)metil)benzamida



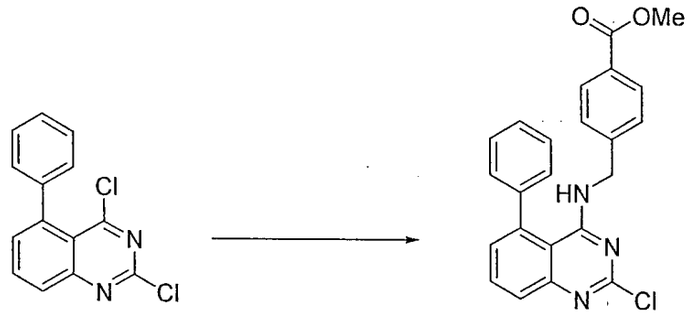
Etapa 1. Preparación de 4-(aminometil)benzoato de metilo



A una solución de ácido 4-(aminometil)benzoico (1 g, 7 mmol) en MeOH (10 ml) se añadió, gota a gota, H_2SO_4 concentrado (1 ml). Tras la finalización de la adición, la mezcla de reacción se calentó hasta 60ºC, temperatura a la que se agitó durante 12 horas. Después de este tiempo, la mezcla de reacción se concentró a presión reducida dando un residuo. El residuo se disolvió en acetato de etilo y después se neutralizó cuidadosamente con una solución de NaOH al 10%. La capa orgánica se separó y se lavó sucesivamente con agua y salmuera. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida, dando 4-(aminometil)benzoato de metilo (2,5 g) en forma de un sólido blanco. CLEM Procedimiento O: tiempo de retención 0,49 min [M+1] = 166,2.

000817

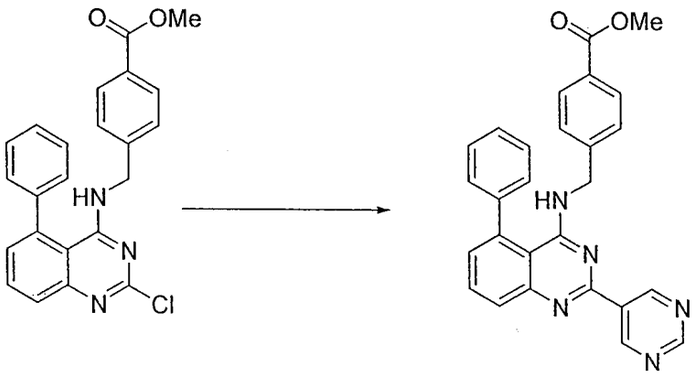
Etapa 2. Preparación de 4-((2-cloro-5-fenilquinazolin-4-ilamino)-metil)benzoato de metilo



A una solución de ,4-dicloro-5-fenilquinazolina (1 g, 4 mmol) en THF (15 ml) se añadió diisopropiletilamina (1,86 ml, 10,9 mmol), seguido por 4-(aminometil)benzoato de metilo (1,10 g, 7,21 mmol). Tras finalizar la adición, la mezcla de reacción se agitó durante 12 horas. Al finalizar este periodo, la mezcla de reacción se diluyó con acetato de etilo y después se lavó sucesivamente con agua y salmuera. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, se filtraron y se concentraron dando un residuo. El residuo se purificó mediante cromatografía en columna ultrarrápida usando acetato de etilo al 6% en éter de petróleo, dando 4-((2-cloro-5-fenilquinazolin-4-ilamino)metil)benzoato de metilo (600 mg) en forma de un sólido blanco. RMN ^1H (400 MHz, $CDCl_3$) δ (ppm): 7,92 (d, *J* = 8,0 Hz, 2H), 7,80 (d, *J* = 8,4 Hz, 1H), 7,70 (t, *J* = 8,0 Hz, 1H), 7,38-7,33 (m, 5H), 7,22 (d, *J* = 7,2 Hz, 1H), 7,02 (d, *J* = 8,0 Hz, 2H), 5,56 (as, 1H), 4,53 (d, *J* = 4,8 Hz, 2H), 3,39 (s, 3H). CLEM Procedimiento O: tiempo de retención 2,12 min [M+1] = 404,0. Procedimiento B HPLC: pureza 97,8%, tiempo de retención 18,17 min.

Etapa 3. Preparación de 4-((5-fenil-2-(pirimidin-5-il)quinazolin-4-ilamino)metil)benzoato de metilo

009818

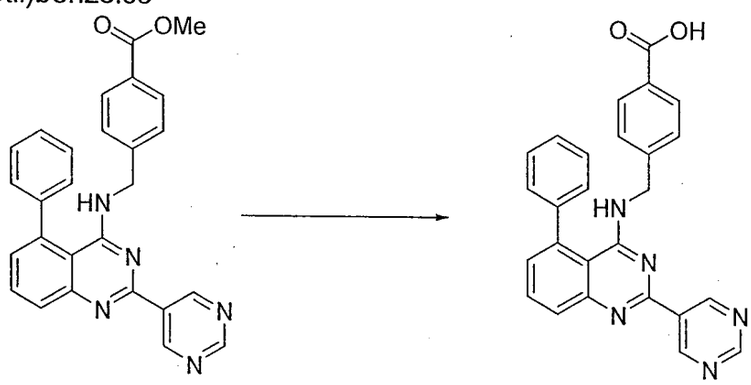


A una solución de 4-((2-cloro-5-fenilquinazolin-4-ilamino)metil)benzoato de metilo (550 mg, 1.36 mmol en DMF (16 ml) y H_2O (0,5 ml) en nitrógeno se añadió éster de pinacol de ácido pirimidin-5-ilborónico (422 mg, 2,04 mmol) y carbonato potásico (377 mg, 2,72 mmol). La mezcla resultante se desgasificó con nitrógeno durante 15 minutos y, después, se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (50 mg, 0,068 mmol). Tras finalizar la adición, la mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se calentó después hasta 110ºC, temperatura a la que se agitó durante 12 horas. Después de este tiempo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente. Una vez a la temperatura prescrita, la mezcla de reacción se inactivó mediante la adición de agua y después se extrajo con acetato de etilo. La capa orgánica se lavó sucesivamente con agua y salmuera. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El concentrado resultante se purificó mediante cromatografía en columna ultrarrápida usando 5% de MeOH en CH_2Cl_2, dando 4-((5-fenil-2-(pirimidin-5-il)quinazolin-4-ilamino)metil)benzoato de metilo (400 mg) en forma de un sólido blancuzco. RMN ^1H (400 MHz, DMSO-d_6) δ (ppm): 9,62 (s, 2H), 9,31 (s, 1H), 7,93-7,86

000819

(m, 4H), 7,54-7,49 (m, 5H), 7,37 (d, *J* = 6,8 Hz, 1H), 7,28 (d, *J* = 8,0 Hz, 2H), 5,94 (t, *J* = 4,8 Hz, 1H), 4,71 (d, *J* = 5,2 Hz, 1H), 3,85 (s, 3H). CLEM (Procedimiento C): tiempo de retención 2,15 min [M+1] = 448,2. Procedimiento B HPLC: pureza 98,5%, tiempo de retención 9,81 min.

Etapa 4. Preparación de ácido 4-((5-fenil-2-(pirimidin-5-il)quinazolin-4-ilamino)metil)benzoico

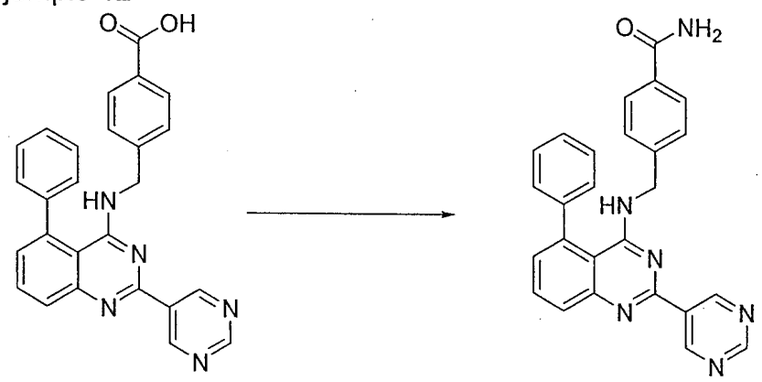


A una solución de 4-((5-fenil-2-(pirimidin-5-il)quinazolin-4-ilamino)metil)benzoato de metilo (400 mg, 0,89 mmol) en MeOH-THF-H_2O (6 ml-6 ml-0,5 ml) se añadió LiOH (112 mg, 2,67 mmol). Tras la finalización de la adición, la mezcla de reacción se calentó hasta 45ºC, temperatura a la que se agitó durante 12 horas. Después de este tiempo, la mezcla de reacción se concentró a presión reducida para eliminar el MeOH y el THF y, después, se acidificó cuidadosamente con HCl 1,5N. El precipitado resultante se recogió mediante filtración, dando ácido 4-((5-fenil-2-(pirimidin-5-il)quinazolin-4-ilamino)metil)benzoico (250 mg) en forma de un sólido blanco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 12,87 (as, 1H), 9,68 (s, 2H), 9,39 (s, 1H), 8,09 (m, 1H), 7,98 (t, *J* = 8,0 Hz, 1H), 7,86 (d, *J* = 8,0 Hz, 2H), 7,53-7,48 (m, 6H), 7,26 (d, *J* = 8,0 Hz, 2H), 6,65 (as, 1H), 4,78 (d, *J* = 5,2 Hz, 2H). CLEM

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Procedimiento O: tiempo de retención 1,73 min [M+1] = 434,2. Procedimiento B HPLC: pureza 98,1%, tiempo de retención 8,24 min.

Etapa 5. Ejemplo 12

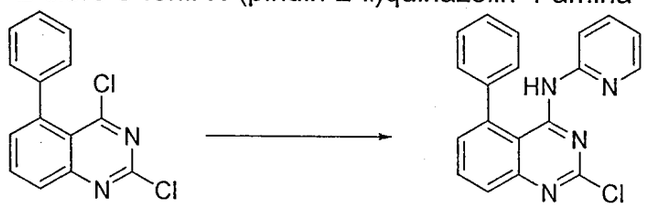


A una solución de ácido 4-((5-fenil-2-(pirimidin-5-il)quinazolin-4-ilamino)metil)benzoico (75 mg, 0,17 mmol), EDC-HCl (40 mg, 0,21 mmol), y HOBt (28 mg, 0,21 mmol) en DMF (4 ml) se añadió diisopropiletilamina (120 µL, 0,69 mmol) seguida por NH_4Cl (37 mg, 0,69 mmol). Tras finalizar la adición, la mezcla de reacción se agitó a temperatura ambiente durante 12 horas y después se diluyó con acetato de etilo. La capa orgánica se lavó sucesivamente con agua y salmuera. La porción orgánica se separó, se secó sobre Na_2SO_4, se filtró y después se concentró a presión reducida. El concentrado resultante se purificó mediante cromatografía en columna ultrarrápida usando acetato de etilo 3% de MeOH en CH_2Cl_2, dando el Ejemplo 12 (25 mg) en forma de un sólido blancuzco. RMN ^1H (400 MHz, DMSO-d_6) δ (ppm): 9,65 (s, 2H), 9,31 (s, 1H), 7,94-7,85 (m, 3H), 7,79 (d, *J* = 8,0 Hz, 2H), 7,52-7,49 (m, 5H), 7,36 (m, 2H), 7,17 (d, *J* = 8,0 Hz, 2H), 5,89 (t, *J* = 4,8 Hz, 1H), 4,66 (d, *J* = 4,8 Hz, 2H). CLEM Procedimiento O: tiempo de retención 1,49 min [M+1] = 433,2. Procedimiento B HPLC: pureza 98,4%,

tiempo de retención 7,52 min.

EJEMPLO 16

2-cloro-5-fenil-N-(piridin-2-il)quinazolin-4-amina



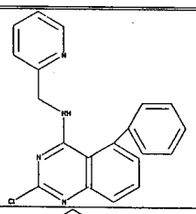
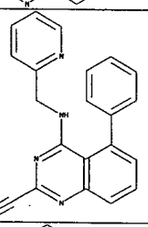
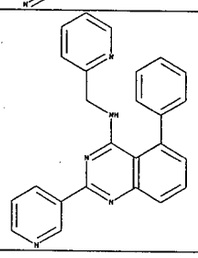
A una suspensión de NaH (13 mg, 0,547 mmol) en THF (2 ml) a 0°C se añadió una solución de 3-aminopiridina (26 mg, 0,273 mmol) en THF (2 ml). Tras finalizar la adición, la mezcla de reacción se agitó a 0°c durante 30 minutos. Al finalizar este periodo se añadió una solución de 2,4-dicloro-5-fenilquinazolina (75 mg, 0,273 mmol) en THF (2 ml). La mezcla de reacción se dejó calentar hasta la temperatura ambiente, a la que se agitó durante 16 horas. Después de este tiempo, la mezcla de reacción se inactivó con una solución acuosa saturada de NH_4Cl y la solución resultante se extrajo con acetato de etilo. La capa orgánica se lavó sucesivamente con agua y salmuera, se secó sobre Na_2SO_4, se filtró y se concentró a presión reducida. El concentrado resultante se purificó mediante cromatografía en columna ultrarrápida usando acetato de etilo 30% en éter de petróleo, dando el Ejemplo 16 (15 mg) en forma de un sólido blanco. RMN ^1H (400 MHz, $CDCl_3$) δ (ppm): 8,53-8,51 (d, *J* = 8,4 Hz, 1H), 8,11-8,09 (dd, *J* = 4,0, 1,2 Hz, 1H), 7,92-7,88 (m, 2H), 7,82-7,78 (t, *J* = 7,6 Hz, 1H), 7,73-7,69 (dt, *J* = 8,0, 1,6 Hz, 1H), 7,62-7,60 (m, 3H), 7,52-7,50 (m, 2H), 7,39-7,37 (d, *J* = 7,2 Hz, 1H), 6,97-6,94 (dd, *J* = 7,2, 4,8 Hz, 1H). CLEM Procedimiento M: tiempo de retención 1,73 min [M+1] = 333,2. Procedimiento B HPLC: pureza 99,7%, tiempo de

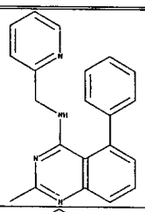
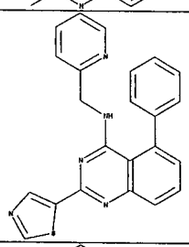
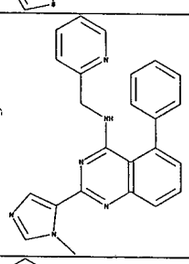
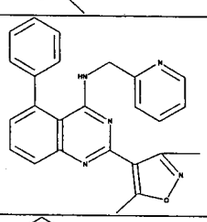
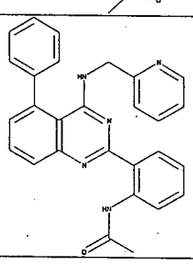
retención 17,30 min.

EJEMPLOS 19 A 58

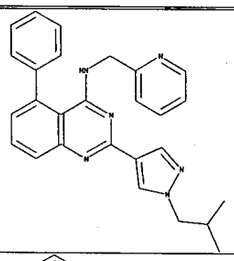
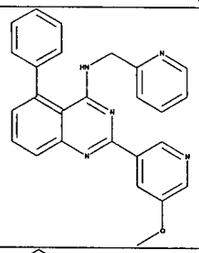
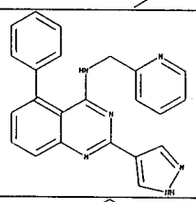
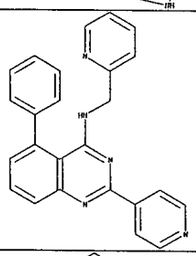
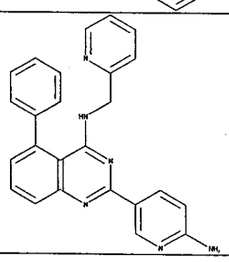
Los Ejemplos 19 a 58 se sintetizaron mediante procedimientos similares descritos en lo que antecede. Los datos de HPLC/EM para cada compuesto se recogieron usando el procedimiento E y la masa molecular se determinó mediante EM (ES) mediante la fórmula m/z- Tanto el tiempo de retención como los datos de EM para los ejemplos se indican en la Tabla 1a, en la que PM= peso molecular.

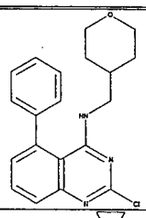
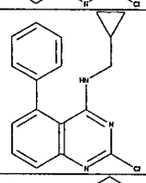
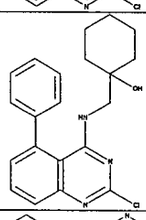
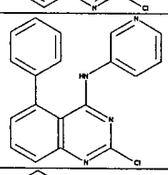
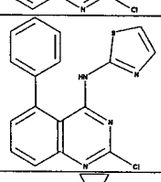
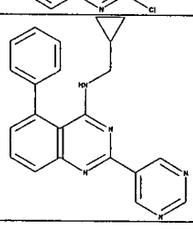
TABLA 1a

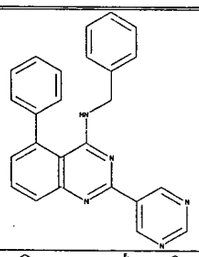
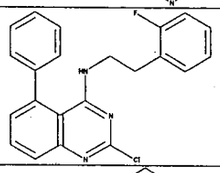
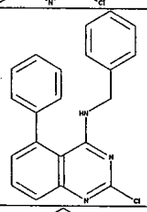
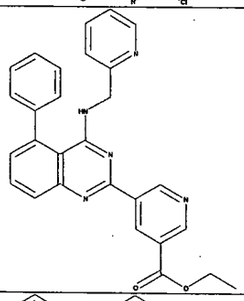
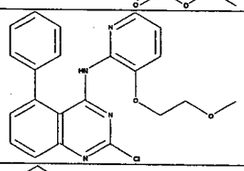
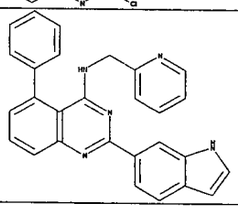
Ejemplo	Estructura	PM	Datos de CLEM	Procedimiento de CLEM
19		346,813	[M+1] 347,0 Tr: 0,95 min	A
20		337,377	[M+1] 338,3 Tr: 0,88 min	D
21		389,452	[M+1] 390,3 Tr: 0,73 min	D

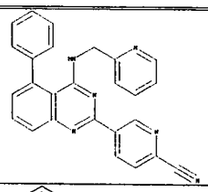
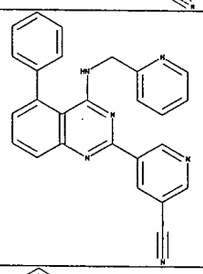
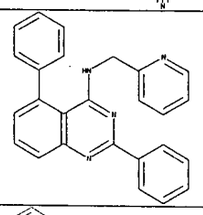
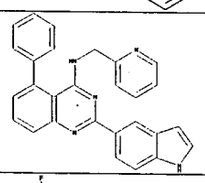
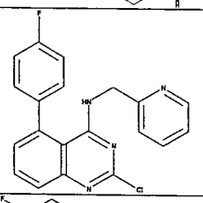
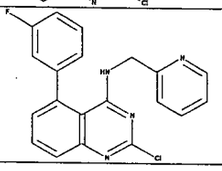
Ejemplo	Estructura	PM	Datos de CLEM	Procedimiento de CLEM
22		326,394	[M+1] 327,1 Tr: 0,65 min	A
23		395,48	[M+1] 396,3 Tr: 0,86 min	D
24		392,456	[M+1] 393,2 Tr: 0,72 min	A
25		407,467	[M+1] 408,2 Tr: 1,525 min	M
26		445,515	[M+1] 446,2 Tr: 1,477 min	M

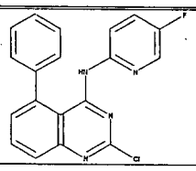
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Ejemplo	Estructura	PM	Datos de CLEM	Procedimiento de CLEM
27		434,536	[M+1] 435,2 Tr: 1,667 min	M
29		419,478	[M+1] 420,2 Tr: 1,631 min	N
30		378,429	[M+1] 379,2 Tr: 1,359 min	M
31		389,452	[M+1] 390,2 Tr: 1,370 min	M
32		404,467	[M+1] 405,2 Tr: 1,298 min	M

Ejemplo	Estructura	PM	Datos de CLEM	Procedimiento de CLEM
34		353,845	[M+1] 354,2 Tr: 1,675 min	O
35		309,793	[M+1] 310,2 Tr: 1,893 min	O
36		367,872	[M+1] 368,2 Tr: 1,857 min	O
37		332,786	[M+1] 333,2 Tr: 1,888 min	N
38		338,814	[M+1] 339,0 Tr: 1,907 min	O
39		353,42	[M+1] 354,2 Tr: 1,626 min	O

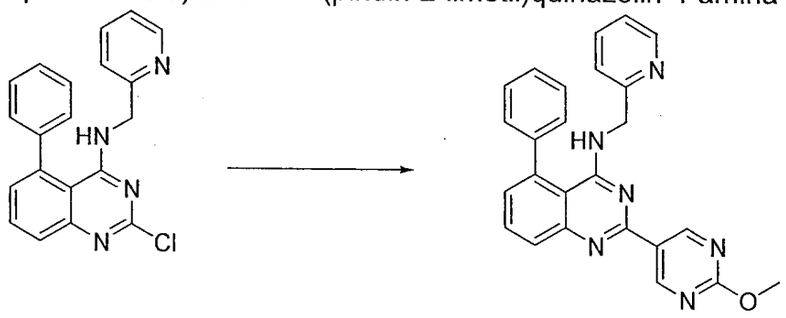
Ejemplo	Estructura	PM	Datos de CLEM	Procedimiento de CLEM
40		389,452	[M+1] 390,2 Tr: 1,810 min	O
41		377,842	[M+1] 378,2 Tr: 2,042 min	O
42		345,825	[M+1] 346,2 Tr: 2,000 min	O
43		461,515	[M+1] 462,2 Tr: 2,138 min	Q
45		406,865	[M+1] 407,2 Tr: 1,656 min	Q
46		427,5	[M+1] 428,2 Tr: 1,622 min	O

Ejemplo	Estructura	PM	Datos de CLEM	Procedimiento de CLEM
47		414,461	[M+1] 415,2 Tr: 2,036 min	M
48		414,461	[M+1] 415,2 Tr: 1,653 min	O
50		388,464	[M+1] 389,2 Tr: 1,605 min	O
51		427,5	[M+1] 428,2 Tr: 1,663 min	O
54		364,803	[M+1] 365,2 Tr: 1,517 min	O
55		364,803	[M+1] 365,2 Tr: 1,530 min	O

Ejemplo	Estructura	PM	Datos de CLEM	Procedimiento de CLEM
58		350,777	[M-1] 349,0 Tr: 3,084 min	P

EJEMPLO 62

2-(2-metoxipirimidin-5-il)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina



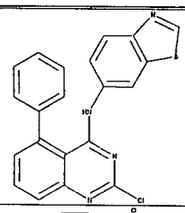
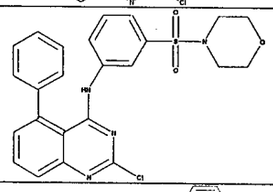
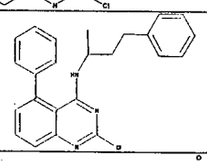
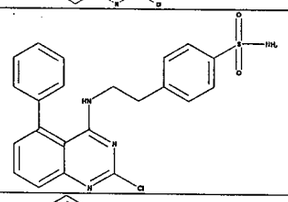
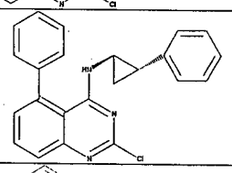
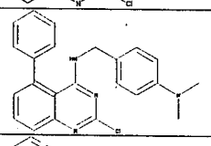
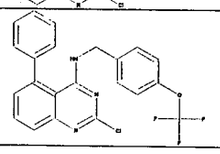
A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (300 mg, 0,87 mmol) en DMF (20 ml) y H_2O (2 ml) en nitrógeno se añadió ácido 2-metoxipiridin-5-ilborónico (199 mg, 1,30 mmol) y carbonato potásico (239 mg, 1,73 mmol). La mezcla resultante se desgasificó con nitrógeno durante 15 minutos y después se añadió tetraquis(trifenilfosfina)paladio (100 mg, 0,086 mmol). Tras finalizar la adición, la mezcla de reacción se desgasificó de nuevo con nitrógeno durante 10 minutos. Tras este tiempo, la mezcla de reacción se calentó a 90ºC, temperatura a la cual se agitó durante 12 horas. Después de este tiempo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente y, después, se inactivó mediante la adición de

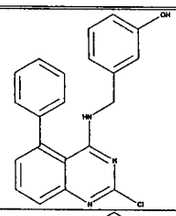
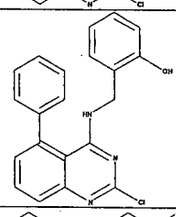
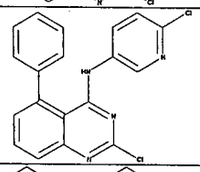
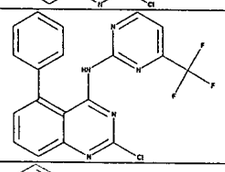
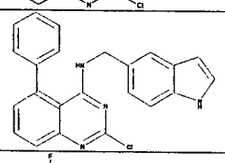
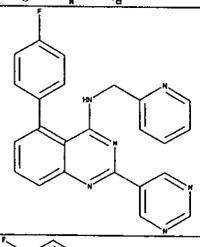
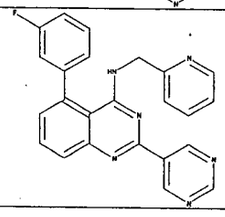
agua. La mezcla de reacción se extrajo con acetato de etilo y la capa orgánica se lavó sucesivamente con agua y salmuera. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El concentrado resultante se purificó mediante HPLC preparativa, dando 2-(2-metoxipirimidin-5-il)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (205 mg) en forma de un sólido blancuzco. Condiciones de la HPLC preparativa: Columna: Sunfire C18 (250 x 19 mm), Fase móvil A: 0,1% de TFA en H_2O, Fase móvil B: CH_3CN, Gradiente: 0 a 40% B durante 35 min, 100% B durante 10 min., Caudal: 14 ml/min, tiempo de retención: 28 min. RMN ^1H (400 MHz, DMSO-d_6) δ (ppm): 9,50 (s, 2H), 8,27 (d, *J* = 4,7 Hz, 1H), 7,92 (d, *J* = 3,6 Hz, 2H), 7,85-7,81 (t, *J* = 8,0 Hz, 1H), 7,60-7,52 (m, 5H), 7,42-7,38 (m, 2H), 7,34-7,31 (m, 1H), 4,83 (d, *J* = 4,2 Hz, 2H), 4,04 (s, 3H). CLEM Procedimiento O: tiempo de retención 1,45 min [M+1] = 421,2. Procedimiento B HPLC: pureza 98,7%, tiempo de retención 5,53 min.

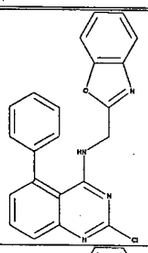
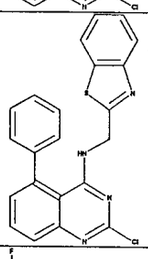
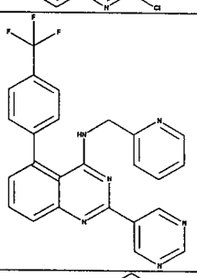
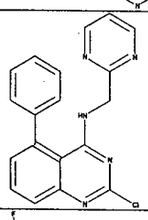
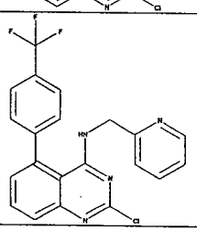
EJEMPLOS 66 a 158

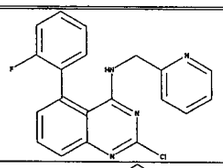
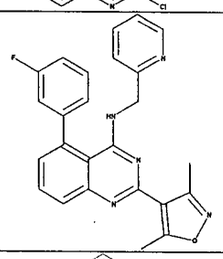
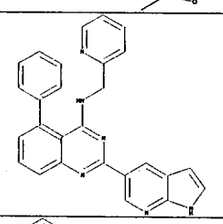
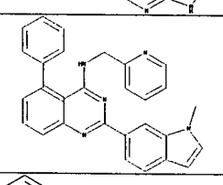
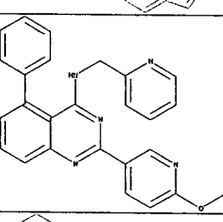
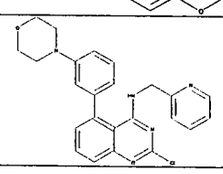
Los Ejemplos 66 a 158 se sintetizaron mediante procedimientos similares descritos en lo que antecede. Los datos de HPLC/EM para cada compuesto se recogieron usando el procedimiento E y la masa molecular se determinó mediante EM (ES) mediante la fórmula m/z- Tanto el tiempo de retención como los datos de EM para los ejemplos se indican en la Tabla 1b, en la que PM= peso molecular.

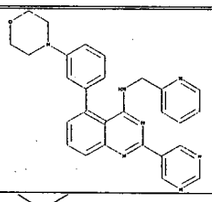
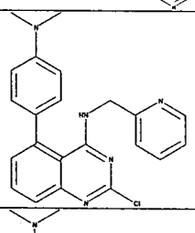
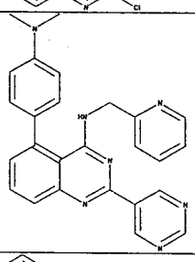
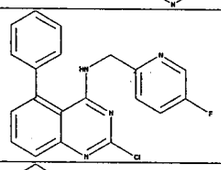
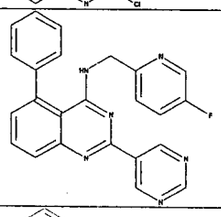
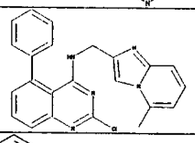
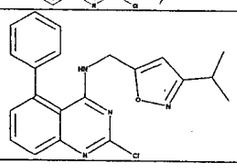
TABLA 1b

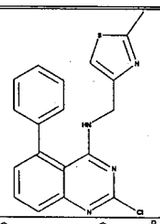
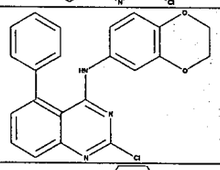
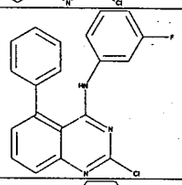
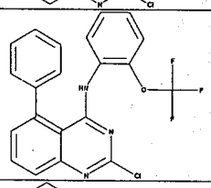
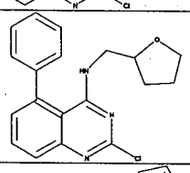
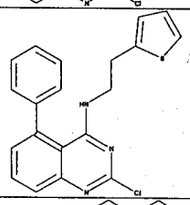
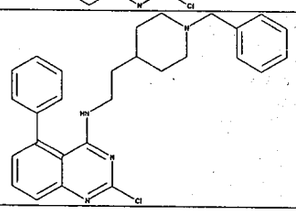
Ejemplo	Estructura	PM	Datos de CLEM	Procedimiento de CLEM
66		388,873	[M-1] 386,8 Tr: 5,82 min	L
67		480,967	[M] 478,7 Tr: 5,75 min	L
68		387,905	[M] 385,9 Tr: 7,09 min	L
69		438,93	[M-1] 436,9 Tr: 4,67 min	L
70		371,862	[M-1] 369,9 Tr: 6,68 min	L
72		388,893	[M] 386,9 Tr: 6,47 min	L
74		429,822	[M-1] 427,8 Tr: 6,83 min	L

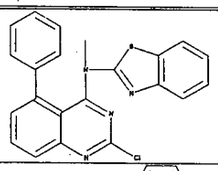
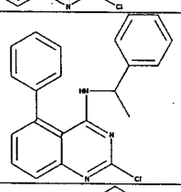
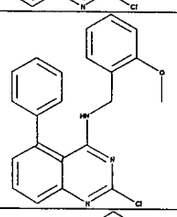
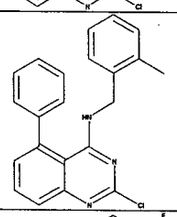
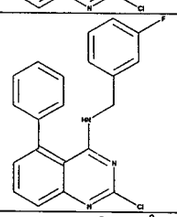
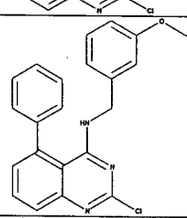
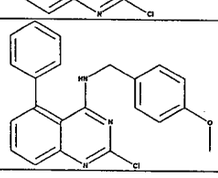
Ejemplo	Estructura	PM	Datos de CLEM	Procedimiento de CLEM
76		361,824	[M-1] 359,9 Tr: 5,06 min	L
77		361,824	[M-1] 359,8 Tr: 5,40 min	L
84		367,231	[M-1] 364,9 Tr: 6,09 min	L
85		401,772	[M-1] 399,8 Tr: 5,42 min	L
87		384,861	[M-1] 382,9 Tr: 5,72 min	L
88		408,43	[M+1] 409,2 Tr: 2,031 min	Q
89		408,43	[M+1] 409,2 Tr: 2,035 min	Q

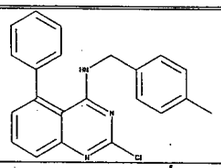
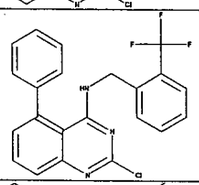
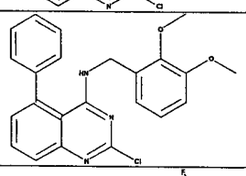
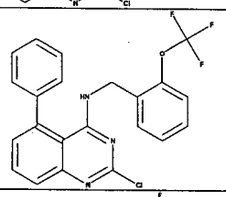
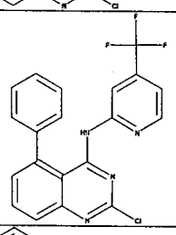
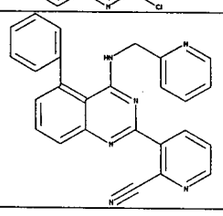
Ejemplo	Estructura	PM	Datos de CLEM	Procedimiento de CLEM
92		386,834	[M+1] 387,0 Tr: 2,102 min	O
93		402,899	[M+1] 403,0 Tr: 2,159 min	O
95		458,438	[M+1] 459,2 Tr: 3,225 min	S
96		347,801	[M+1] 348,2 Tr: 1,706 min	O
97		414,811	[M+1] 415,2 Tr: 2,016 min	Q

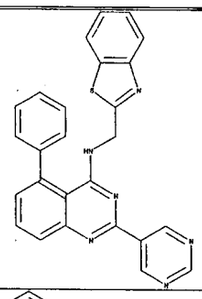
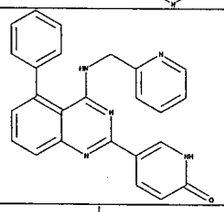
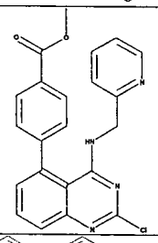
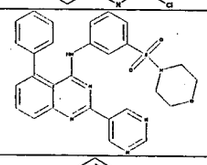
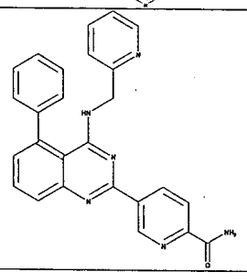
Ejemplo	Estructura	PM	Datos de CLEM	Procedimiento de CLEM
99		364,803	[M+1] 365,2 Tr: 2,010 min	Q
102		425,458	[M+1] 426,2 Tr: 3,298 min	S
103		428,488	[M+1] 429,2 Tr: 2,030 min	Q
104		441,526	[M+1] 442,2 Tr: 1,755 min	O
105		419,478	[M+1] 420,2 Tr: 3,957 min	R
106		431,917	[M+1] 432,2 Tr: 1,902 min	Q

Ejemplo	Estructura	PM	Datos de CLEM	Procedimiento de CLEM
107		475,544	[M+1] 476,2 Tr: 1,971 min	Q
108		389,881	[M+1] 390,2 Tr: 2,006 min	Q
109		433,508	[M+1] 434,2 Tr: 2,084 min	Q
110		364,803	[M+1] 365,0 Tr: 1,866 min	O
111		408,43	[M+1] 409,2 Tr: 2,099 min	Q
113		399,876	[M] 400,0 Tr: 3,09 min	L
114		378,855	[M] 379,0 Tr: 3,68 min	L

Ejemplo	Estructura	PM	Datos de CLEM	Procedimiento de CLEM
117		366,867	[M] 366,9 Tr: 3,32 min	L
118		389,834	[M] 388,2 Tr: 6,00 min	L
119		349,789	[M] 348,1 Tr: 6,48 min	L
122		415,796	[M-1] 414,1 Tr: 6,69 min	L
126		339,819	[M-1] 338,2 Tr: 5,28 min	L
127		365,879	[M-1] 364,2 Tr: 6,30 min	L
128		457,01	[M-1] 455,2 Tr: 5,07 min	L

Ejemplo	Estructura	PM	Datos de CLEM	Procedimiento de CLEM
129		402,899	[M-1] 401,1 Tr: 6,17 min	L
130		359,851	[M-1] 358,2 Tr: 6,46 min	L
131		375,851	[M-1] 374,2 Tr: 6,31 min	L
132		359,851	[M-1] 358,1 Tr: 6,50 min	L
133		363,815	[M] 362,1 Tr: 6,16 min	L
134		375,851	[M-1] 374,2 Tr: 6,06 min	L
135		375,851	[M-1] 374,3 Tr: 6,06 min	L

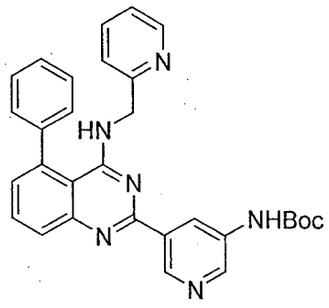
Ejemplo	Estructura	PM	Datos de CLEM	Procedimiento de CLEM
136		359,851	[M-1] 358,2 Tr: 6,57 min	L
137		413,823	[M-1] 412,1 Tr: 6,59 min	L
138		405,877	[M+1] 406,1 Tr: 6,03 min	L
139		429,822	[M-1] 428,1 Tr: 6,76 min	L
143		400,784	[M-1] 399,1 Tr: 6,92 min	L
148		414,461	[M+1] 415,2 Tr: 1,685 min	O

Ejemplo	Estructura	PM	Datos de CLEM	Procedimiento de CLEM
149		446,526	[M+1] 447,0 Tr: 3,991 min	S
150		405,451	[M+1] 406,2 Tr: 1,347 min	O
152		404,849	[M+1] 405,2 Tr: 1,909 min	Q
154		524,594	[M+1] 525,2 Tr: 2,041 min	Q
158		432,477	[M+1] 433,0 Tr: 1,455 min	O

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EJEMPLO 159

5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-ilcarbamato de terc-butilo

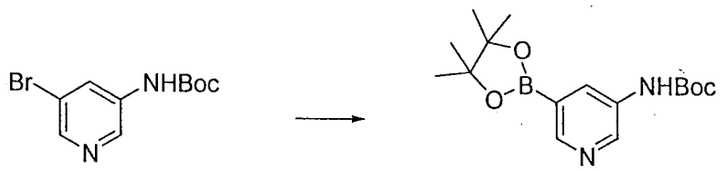


Etapa 1: Preparación de 5-bromopiridin-3-ilcarbamato de terc-butilo

A 5-bromopiridin-3-amina (2,00 g, 11,5 mmol) en THF (25 ml) se añadió hexametildisilazida sódica (25,4 ml, 25,4 mmol, 1 M en THF) y la mezcla de reacción se agitó a temperatura ambiente durante 20 minutos. Lentamente se añadió Boc-anhídrido (2,52 ml, 15,6 mmol) en THF (10 ml) y la mezcla de reacción se agitó durante 24 horas adicionales a temperatura ambiente. Se añadió HCl 0,1M (30 ml) y la mezcla de reacción se extrajo con acetato de etilo. Los extractos orgánicos combinados se lavaron sucesivamente con agua y salmuera. La capa orgánica se secó, se filtró y se concentró a presión reducida, dando 5-bromopiridin-3-ilcarbamato de terc-butilo (2,5 g, 81%), que se usó sin purificación adicional. CLEM Procedimiento 0018: tiempo de retención 1,84 min, [M+1] = 275,0 RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,82 (s, 1H), 8,57 (d, 1H, J = 2,4Hz), 8,30 (d, 1H, J = 2Hz), 8,18 (s,1H), 1,49 (s, 9H).

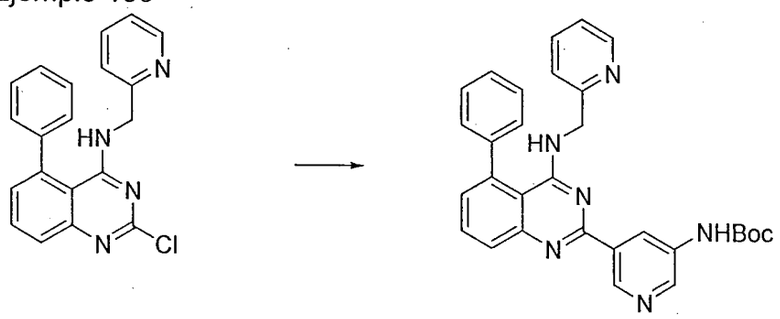
Etapa 2: Preparación de 5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-3-piridin-

3-ilcarbamato de terc-butilo



Una mezcla de 5-bromopiridin-3-ilcarbamato de terc-butilo (0,8 g, 2,9 mmol), bis(pinacolato)diboro (0,82 g, 3,2 mmol) y acetato potásico (0,86 g, 8,7 mmol) en 1,4-dioxano (15 ml) se desgasificó con nitrógeno durante 15 minutos. Después de este tiempo se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio(II) diclorometano (0,12 g, 0,1 mmol) y la mezcla se desgasificó de nuevo durante 10 minutos con nitrógeno. Tras finalizar este periodo, la mezcla de reacción se calentó en el microondas a 120ºC durante 45 minutos. Después de este tiempo, la mezcla de reacción se filtró a través de celite y el filtrado se concentró a presión reducida proporcionando 5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-ilcarbamato de terc-butilo (1,7 g), que se usó sin purificación adicional.

Etapa 3. Ejemplo 159

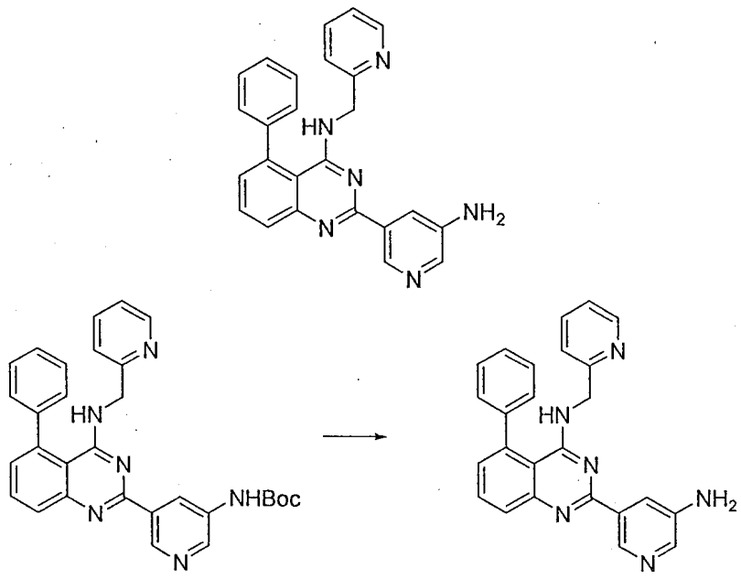


A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (1,2 g, 3,4 mmol) en 1,4-dioxano (10 ml) y H_2O (2,5 ml) en nitrógeno se

añadió 5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-ilcarbamato de terc-butilo (1,7 g, 5,3 mmol), y carbonato potásico (1,4 g, 10 mmol). La mezcla se desgasificó con nitrógeno durante 15 minutos y, después, se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (0,25 mg, 0,3 mmol). Tras finalizar la adición, la mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. Después de este tiempo, la mezcla de reacción se agitó a 90ºC durante 16 horas y después se dejó enfriar hasta la temperatura ambiente. Una vez a la temperatura prescrita, la mezcla de reacción se inactivó mediante la adición de agua y después se transfirió a un embudo de separación. La capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida, dando un residuo. El residuo se purificó mediante cromatografía en columna en gel de sílice usando una mezcla de diclorometano/metanol, dando el Ejemplo 159 (0,9 g, rendimiento del 52%) en forma de un sólido marrón. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,73 (a s, 1H); 9,25 (d, 1H, J = 2Hz); 8,95 (s, 1H); 8,76 (s, 1H); 8,25 (d, 1H, J = 4HZ); 7,91-7,80 (m, 2H); 7,73 (t, 1H, J = 8Hz); 7,60-7,50 (m, 5H); 7,39-7,29 (m, 2H); 7,25 (t, 1H, J = 10Hz); 6,83 (a s, 1H); 4,74 (d, 2H, J = 3,6 Hz); 1,54 (s, 9H). CLEM Procedimiento W: tiempo de retención 2,21 min, [M+1] = 505,2; HPLC Procedimiento K: pureza 97,7%, tiempo de retención = 15,80 min.

EJEMPLO 160

2-(5-aminopirimidin-3-il)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina

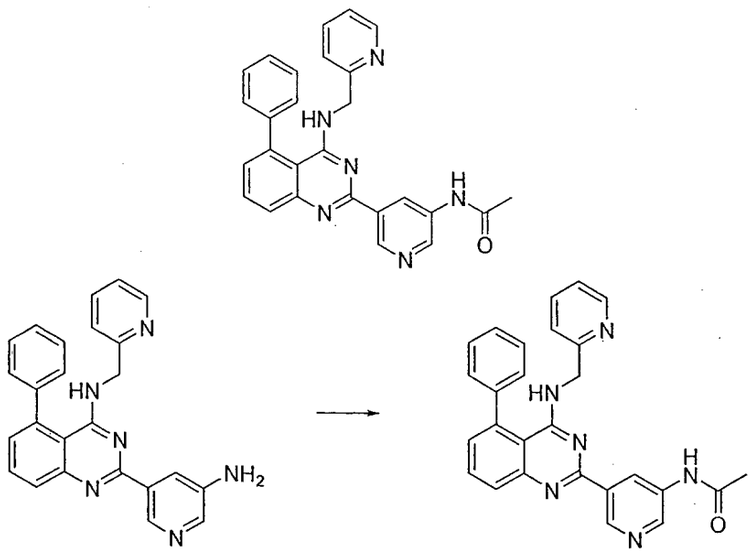


A una solución del ejemplo 159 (750 mg, 1,48 mmol) en DCM (5 ml) a 0ºC se añadió HCl 1,5M en dioxano (1,5M). Tras finalizar la adición, la mezcla de reacción se agitó durante 1 hora y después se concentró dando un residuo. El residuo se purificó mediante combiflash usando 3% de metanol en DCM, dando el ejemplo 160 (560 mg, rendimiento del 93%) en forma de un sólido blancuzco. RMN ^{1}H (400 MHz, DMSO-d_6) δ: 8,84 (s, 1H); 8,24 (d, 1H, J = 3,6Hz): 8,04 (s, 1H); 8,00 (s, 1H); 7,89-7,79 (m, 2H); 7,72 (t, 1H, J = 7,2Hz); 7,62-7,48 (m, 5H); 7,35-7,22 (m, 3H); 6,78 (s, 1H); 5,47 (s, 2H); 4,73 (d, 12H, J = 3,6Hz); CLEM Procedimiento X: tiempo de retención 1,91 min, [M+1] 405,2

HPLC Procedimiento A1: pureza 99,3%, tiempo de retención = 6,84 min.

EJEMPLO 161

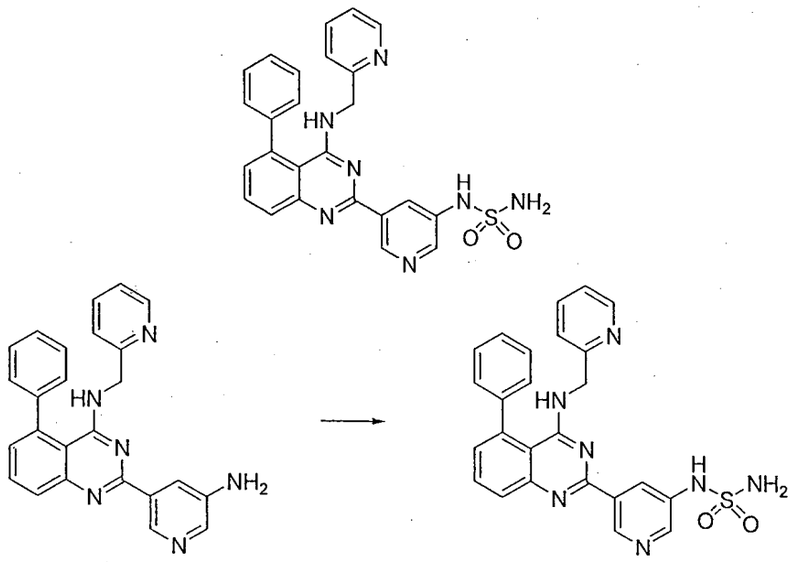
N-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)acetamida



A una solución del ejemplo 160 (0,2 g, 0,5 mmol) en acetona (20 ml) se añadió cloruro de acetilo (0,2 ml, 0,55 mmol) y carbonato potásico (0,2 g, 1,5 mmol). Tras finalizar la adición, la mezcla de reacción se agitó a temperatura ambiente durante 4 horas. Después de este tiempo, la mezcla de reacción se filtró a través de celite y el filtrado se concentró, dando un residuo. El residuo se diluyó con EtOAc y la porción orgánica se lavó con bicarbonato sódico saturado (10 ml). La capa orgánica se secó y después se purificó mediante cromatografía en columna en gel de sílice usando diclorometano/metanol como disolvente obteniendo el Ejemplo 161 (180 mg, 82%) en forma de un sólido blanco. RMN ^{1}H (400 MHz, DMSO-d_6) δ: 10,34 (s, 1H); 9,31 (d, 1H, J = 2,4Hz); 8,96 (d, 2H, J = 5,2Hz), 8,24 (d, 1H, J = 4,8Hz), 7,93-7,80 (m, 2H), 7,73 (dt, 1H, J = 2,4Hz,7,6Hz), 7,60-7,47 (m, 5H), 7,38-7,28 (m, 2H), 7,24 (t, 1H, J = 9,2Hz), 6,85 (a s, 1H), 4,74 (d, 2H, J = 4Hz), 2,13 (s, 3H). CLEM Procedimiento W: tiempo de retención 1,85 min [M+1] = 447,2. HPLC Procedimiento A1: pureza 98,5%, tiempo de retención = 7,20 min.

EJEMPLO 162

N-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)sulfamida

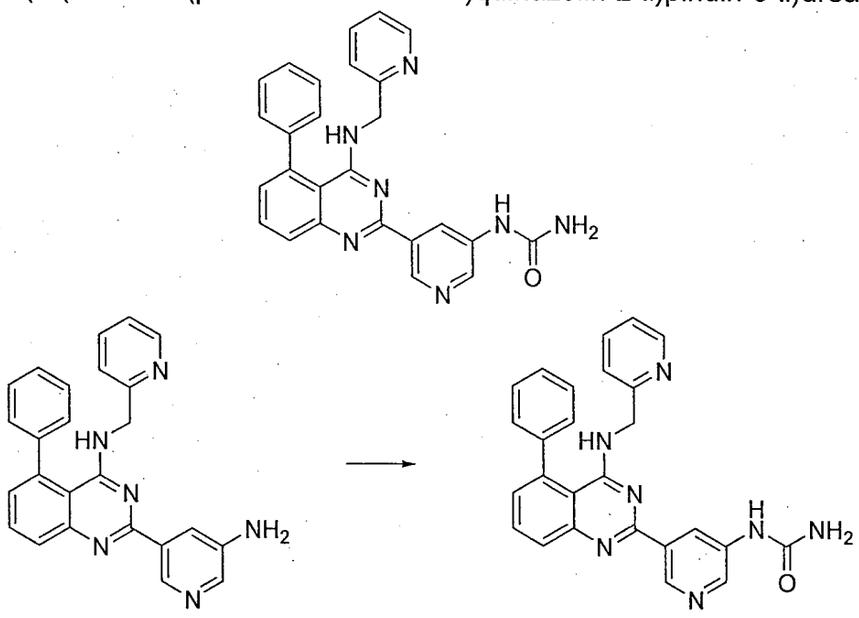


A una solución de clorosulfonilisocianato (0,021 ml, 0,24 mmol) en DCM (4 ml) se añadió t-BuOH (0,023 ml, 0,24 mmol) a temperatura ambiente. Tras finalizar la adición, la mezcla de reacción se agitó durante 10 minutos. Después de este tiempo, se añadió TEA (0,05 ml, 0,3 mmol), seguido por una solución del Ejemplo 160 (0,1 g, 0,24 mmol) en DCM. La mezcla de reacción se agitó durante 3 horas adicionales y después se lavó con una solución de Na_2CO_3. La capa acuosa se extrajo con acetato de etilo. Los extractos orgánicos combinados se secaron, se concentraron a presión reducida y se purificaron mediante cromatografía en columna en gel de sílice usando mezcla de diclorometano/metanol, dando el Ejemplo 162 (0,040 g, rendimiento del 34%). RMN ^{1}H (400 MHz, DMSO-d_6) δ: 9,88 (s, 1H); 9,30 (s, 1H); 8,61 (a s, 1H); 8,56 (d, 1H, J = 2,4Hz); 8,24 (d, 1H, J = 4,4Hz); 7,91-7,80 (m, 2H); 7,73 (dt, 1H, J = 7,6Hz); 7,61-7,49 (m, 5H); 7,38-7,29 (m, 4H); 7,24 (t, 1H, J = 5,6Hz); 6,86 (a t, 1H, J = 3,6Hz); 4,74 (d, 2H, J = 4Hz). CLEM

Procedimiento X: tiempo de retención 1,81 min [M+1] = 484,2. HPLC Procedimiento A1: pureza 97,1%, tiempo de retención = 7,83 min.

EJEMPLO 163

1-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)urea



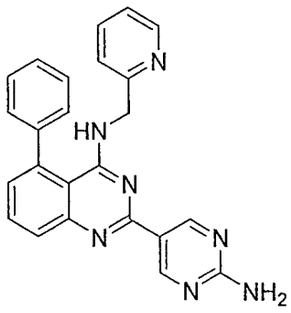
A una solución del Ejemplo 160 (0,2 g, 0,5 mmol) en DCM a 0ºC se añadió clorosulfonilisocianato (0,081 ml, 0,90 mmol). La suspensión espesa resultante se agitó a temperatura ambiente durante 4 horas y después se añadieron 2 ml de HCl 1,5N. Tras finalizar la adición, la mezcla de reacción se calentó hasta 40ºC, temperatura a la que se agitó durante 2 horas adicionales. La solución resultante se neutralizó con una solución de Na_2CO_3 saturada y la porción acuosa se extrajo con DCM. Los extractos orgánicos combinados se secaron, se concentraron y se purificaron mediante HPLC preparativa 5% de metanol en diclorometano, dando el Ejemplo 163 (0,040 g, rendimiento del 18%). RMN ^{1}H (400 MHz, DMSO-d_6) δ: 9,19 (s, 1H); 8,94 (s, 1H); 8,83 (s, 1H); 8,76 (d, 1H, J = 2,4Hz); 8,24 (d, 1H, J = 4,8Hz); 7,90-7,80

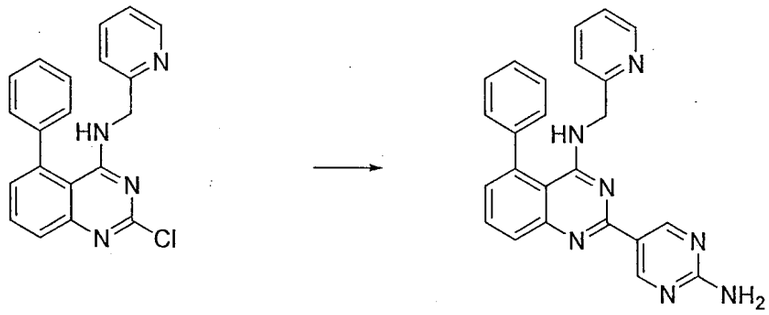
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(m, 2H); 7,73 (t, 1H, *J* = 8,4Hz); 7,60-7,50 (m, 5H); 7,38-7,29 (m, 2H); 7,24 (t, 1H, *J* = 5,2Hz); 6,83 (a t, 1H, *J* = 4Hz); 6,07 (a s, 2H); 4,74 (d, 2H, *J* = 4Hz). CLEM Procedimiento T: tiempo de retención 1,43 min [M+1] = 448,0. HPLC Procedimiento A1: pureza 98,8 %, tiempo de retención = 6,95 min.

EJEMPLO 164

2-(2-aminopirimidin-5-il)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina





A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,7 g, 2,02 mmol) en 1,4-dioxano (30 ml) y H_2O (5 ml) en nitrógeno se añadió éster de ácido 1-aminopirimidin-5-ilborónico (670 g, 3,03 mmol) y carbonato potásico (0,55 g, 4,04 mmol). Tras la finalización de la adición, la mezcla se desgasificó con nitrógeno durante 15 minutos y, después, se añadió el

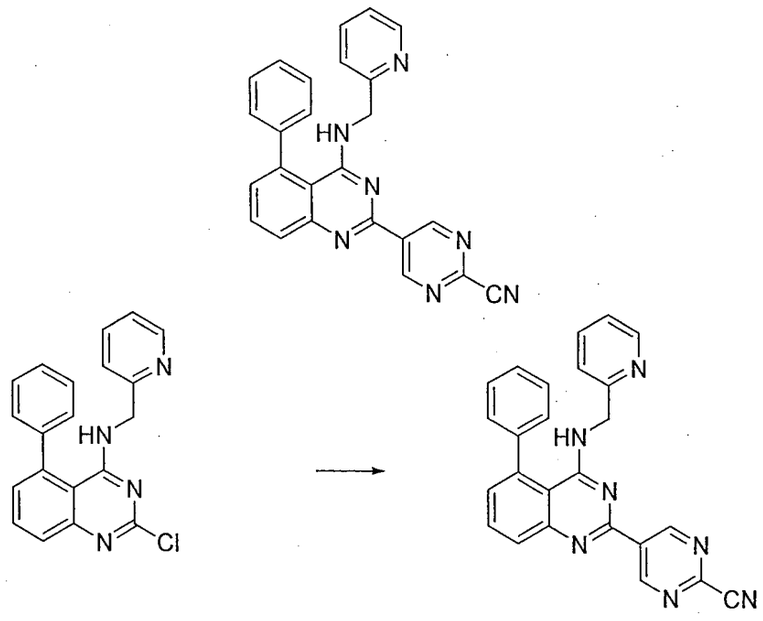
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complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (0,147 mg, 0,20 mmol). La mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. Después de este tiempo, la mezcla de reacción se calentó hasta 90ºC, temperatura a la cual se agitó durante 16 horas. Al finalizar este periodo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente y después se inactivó mediante la adición de agua. La mezcla de reacción se transfirió a un embudo de separación y la capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El concentrado resultante se purificó mediante cromatografía en columna en gel de sílice usando una mezcla de diclorometano/metanol como eluyente, dando el Ejemplo 164 (0,42 g, rendimiento del 52%) en forma de un sólido marrón. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,20 (s, 2H), 8,23 (d, 1H, J = 4,8 Hz), 7,78 (d, 2H, J = 2,4 Hz), 7,77-7,70 (m, 1H), 7,60-7,57 (m, 5H), 7,34-7,30 (m, 1H),7,26-7,20 (m, 2H), 7,18-7,13 (a s, 2H), 6,76 (a s, 1H), 4,67 (d, 2H, J = 4,0 Hz); CLEM Procedimiento U: tiempo de retención 1,38 min, [M+1] = 406; HPLC Procedimiento A1: pureza 99,5 %, tiempo de retención = 6,74 min.

EJEMPLO 165

5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)pirimidin-2-carbonitrilo

000848

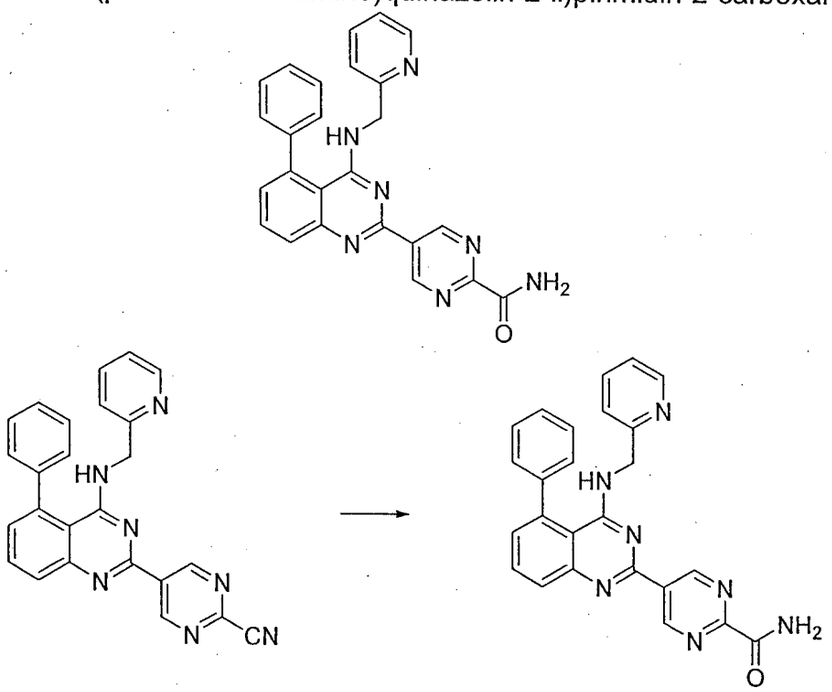


A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,22 g, 0,65 mmol) en 1,4-dioxano (10 ml) y H_2O (2 ml) en nitrógeno se añadió éster de ácido 2-cianopirimidin-5-ilborónico (0,22 g, 0,97 mmol) y carbonato potásico (0,18 g, 1,30 mmol). Tras finalizar la adición, la mezcla se desgasificó con nitrógeno durante 15 minutos. Después de este tiempo se añadió el complejo cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (0,048 mg, 0,06 mmol) y la mezcla de reacción se desgasificó de Nuevo con nitrógeno durante 10 minutos. Después de este tiempo, la mezcla de reacción se agitó y se calentó hasta 90ºC, temperatura a la cual se agitó durante 16 horas. Al finalizar este periodo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente y después se inactivó mediante la adición de agua. La mezcla de reacción se transfirió a un embudo de separación y la capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron

sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El concentrado resultante se purificó mediante cromatografía en columna en gel de sílice usando una mezcla de diclorometano/metanol como eluyente, dando el Ejemplo 165 (0,13 g, rendimiento del 49 %) en forma de un sólido marrón. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,86 (s, 2H), 8,22 (d, 1H, J =6,4 Hz), 7,94 (dd, 1H, J =1,6 Hz J =8,4 Hz), 7,89 (dd, 1H, J = 3,2 Hz, J =11,2 Hz), 7,74 (dt, 1H, J =1,6 Hz, 8 Hz,), 7,63-7,50 (m, 5H),7,40-7,32 (m, 2H), 7,25 (dd, 1H, J =5,2 Hz, 6,8 Hz), 7,08 (a t, 1H, J = 4Hz), 4,76 (d, 2H, J =4,4 Hz). CLEM Procedimiento U: tiempo de retención 1,85 min, [M+1] = 416,0; HPLC Procedimiento A4: pureza 97,6%, tiempo de retención = 23,30 min.

EJEMPLO 166

5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)pirimidin-2-carboxamida

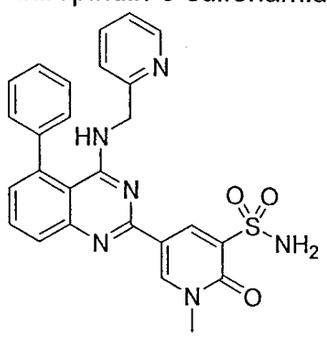


A una solución del Ejemplo 165 (0,115 g, 0,270 mmol) en THF se

añadió NaOH (0,044 g, 1,1 mmol) y agua. Tras finalizar la adición, la mezcla de reacción se enfrió hasta 0ºC y, gota a gota, se añadió peróxido de hidrógeno (0,037 g, 1,1 mmol). La mezcla de reacción se agitó a temperatura ambiente durante 2 horas y después se concentró dando un residuo. El residuo se diluyó con agua y la fase acuosa se extrajo con acetato de etilo. Los extractos orgánicos combinados se secaron y se concentraron. La mezcla resultante se purificó mediante TLC preparatoria usando una mezcla de diclorometano/metanol como eluyente, dando el ejemplo 166 (0,075 g, rendimiento del 63 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ: 9,82 9s, 2H); 8,35 (d, 1H, J = 4Hz); 3,28 (s, 1H); 7,96 (dd, 1H, J = 0,8, 8,4Hz): 7,85 (t, 1H, J = 7,2Hz); 7,74 (dt, 1H, J = 1,4, 7,6Hz); 7,56-7,48 (m, 5H); 7,38 (dd, 1H, J = 0,8, 7,8Hz); 7,31-7,22 (m, 2H); 4,75 (d, 2H, J = 4Hz). CLEM Procedimiento Y: tiempo de retención 1,81 min [M+1] = 434,2. HPLC Procedimiento A1: pureza 96,1 %, tiempo de retención = 9,30 min.

EJEMPLO 167

1.metil-2-oxo-5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)-1,2-dihidropiridin-3-sulfonamida

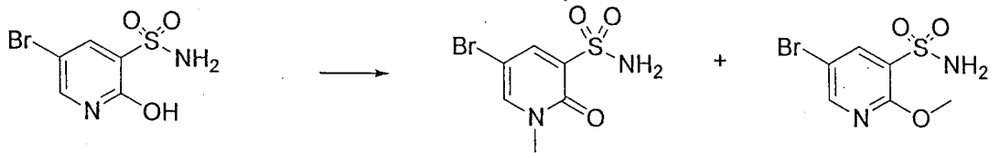


Etapa 1. Preparación de 5-bromo-2-hidroxipiridin-3-sulfonamida



Una solución de 5-bromopiridin-2-ol (0,5 g, 2,8 mmol) en ácido clorosulfónico (10 ml) se calentó hasta 150 °C durante 16 horas. Después de este tiempo, la mezcla de reacción se añadió gota a gota a una solución preenfriada de amoniaco acuoso (100 ml) a 0ºC. La mezcla resultante se agitó durante 1 hora. La capa acuosa se extrajo después con acetato de etilo (150 ml), se secó y se concentró dando un residuo. El residuo se purificó mediante cromatografía ISCO usando 3% de metanol en DCM, dando 5-bromo-2-hidroxipiridin-3-sulfonamida (210 mg). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 12,67 (a s, 1H); 8,03 (d, 1H, J = 2,8Hz); 7,98 (d, 1H, J = 2,8Hz); 7,11 (s, 1H). CLEM Procedimiento U: tiempo de retención 1,85 min [M+1] = 253,0.

Etapa 2. Preparación de 5-bromo-2-metoxipiridin-3-sulfonamida

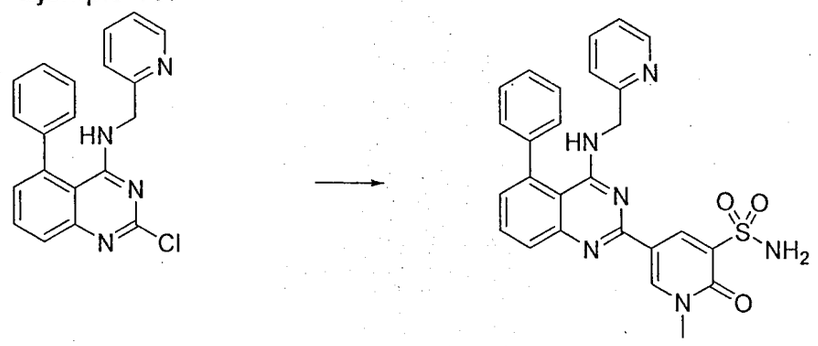


A una solución de 5-bromo-2-hidroxipiridin-3-sulfonamida (0,5 g, 1,9 mmol) en MeOH/DCM (15 ml, 1:1) a -10ºC se añadió una solución de trimetilsilildiazometano (2M, 1,97 ml, 3,9 mmol). Tras finalizar la adición, la mezcla de reacción se concentró y el residuo resultante se purificó mediante cromatografía en columna usando metanol y $CHCl_3$ a 5-bromo-1-metil-2-oxo-1,2-dihidropiridin-3-sulfonamida, rendimiento de 5-bromo-1-metil-2-oxo-1,2-

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dihidropiridin-3-sulfonamida (280 mg, rendimiento del 53 %) y 5-bromo-2-metoxipiridin-3-sulfonamida (180 mg, rendimiento del 34%). Datos para 5-bromo-1-metil-2-oxo-1,2-dihidropiridin-3-sulfonamida: RMN ^{1}H (400 MHz, DMSO-d_6) δ: 8,42 (d, 1H, J = 2,8Hz); 7,99 (d, 1H, J = 2,8Hz); 7,14 (s, 1H); 3,52 (s, 3H). Datos para 5-bromo-2-metoxipiridin-3-sulfonamida: RMN ^{1}H (400 MHz, DMSO-d_6) δ: 8,54 (d, 1H, J = 2,4Hz); 8,17 (d, 1H, J = 2,4Hz); 7,51 (s, 1H); 4,00 (s, 3H).

Etapa 3: Ejemplo 167



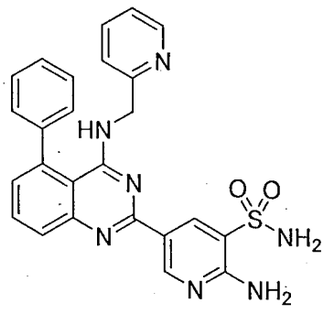
Una solución agitada de 5-bromo-1-metil-2-oxo-1,2-dihidropiridin-3-sulfonamida (0,08 g, 0,3 mmol) en dioxano:DMF (6 ml: 1 ml) se desgasificó durante 10 minutos con argón. Al finalizar este periodo se añadieron Pd(trifenilfosfina)$_4$ (34 mg, 0,03 mmol) y hexametldiestaño (0,17 g, 0,53 mmol). La mezcla de reacción se agitó a temperatura ambiente durante 16 horas y después se añadió 2-cloro-5-fenil-N-(piridin-2ilmetil)quinazolin-4-amina (0,1 g, 0,3 mmol). Tras finalizar la adición, la mezcla de reacción se calentó hasta 100ºC, temperatura a la que se agitó durante 16 horas adicionales. Se formó un precipitado y la suspensión espesa resultante se filtró. El filtrado se concentró y se purificó mediante cromatografía en columna en gel de sílice usando mezcla de diclorometano/metanol como

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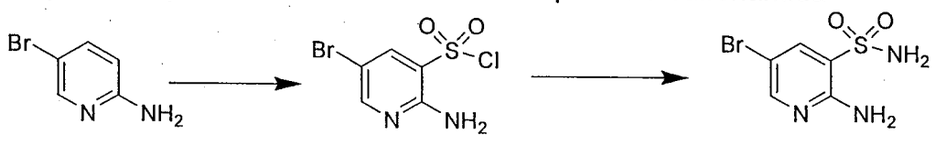
eluyente obteniendo el Ejemplo 167 (15 mg, rendimiento del 13%). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,06 (s, 1H); 9,02 (s, 1H); 8,25 (d, 1H, J = 4Hz); 7,86-7,78 (m, 2H); 7,73 (dt, 1H, J = 1,6, 7,6Hz); 7,60-7,48 (m, 5H); 7,31-7,22 (m, 3H); 7,09 (a s, 2H); 6,79 (t, 1H, J =4Hz); 4,72 (d, 2H, J = 4Hz); 3,72 (s, 3H). CLEM Procedimiento U: tiempo de retención 1,35 min, [M+1] = 499,2; HPLC Procedimiento A1: pureza 96,2 %, tiempo de retención = 6,10 min.

EJEMPLO 168

2-amino-5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-sulfonamida



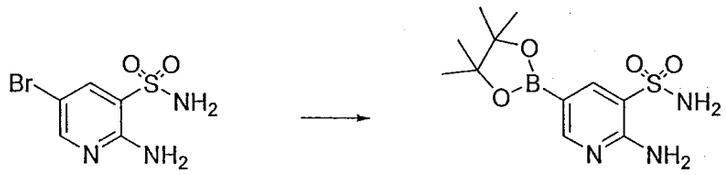
Etapa 1. Preparación de 2-amino-5-bromopiridin-3-sulfonamida



A una solución de ácido clorosulfónico (20 ml) a 01C se añadió 2-amino-5-bromopiridina (5,0 g, 0,029 mmol) en porciones. Tras finalizar la adición, la mezcla de reacción se calentó hasta reflujo, momento en el cual se agitó durante 16 horas. Después de este tiempo, la mezcla de reacción se dejó

enfriar hasta la temperatura ambiente. Una vez a la temperatura prescrita, la mezcla de reacción se vertió gota a gota en una solución de hidróxido amónico acuoso. La mezcla resultante se extrajo con acetato de etilo. Las porciones orgánicas combinadas se elevaron con una solución de salmuera, se secaron sobre Na_2SO_4 y se concentraron a presión reducida, dando 2-amino-5-bromopiridin-3-sulfonamida (4,7 g, 65%), que se usó sin purificación adicional. CLEM Procedimiento Y: tiempo de retención 0,5 min [M+1] = 250,8

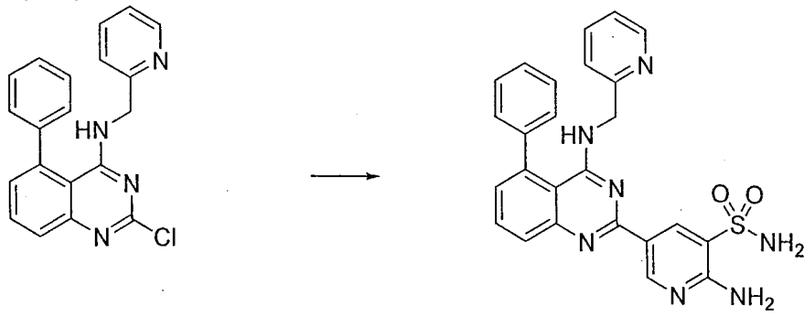
Etapa 2. Preparación de 2-amino-5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-sulfonamida que se usó sin purificación adicional



Una mezcla de 5-bromo-2-aminopiridin-3-sulfonamida (2,0 g, 7,9 mmol), bis(pinacolato)diboro (3,0 g, 12 mmol) y acetato potásico (2,3 g, 23 mmol) en 1,4-dioxano (15 ml) se desgasificó con nitrógeno durante 20 minutos. Después de este tiempo se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio(II) diclorometano (0,29 g, 0,36 mmol) y la mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se calentó hasta 100ºC, temperatura a la que se agitó durante 12 minutos. Al finalizar este periodo, la mezcla de reacción se filtró a través de celite y el filtrado se concentró a presión reducida proporcionando 2-amino-5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-sulfonamida (1 g), que se usó sin purificación adicional. CLEM

Procedimiento X: tiempo de retención 1,29 min [M+1] = 300.

Etapa 3. Ejemplo 168

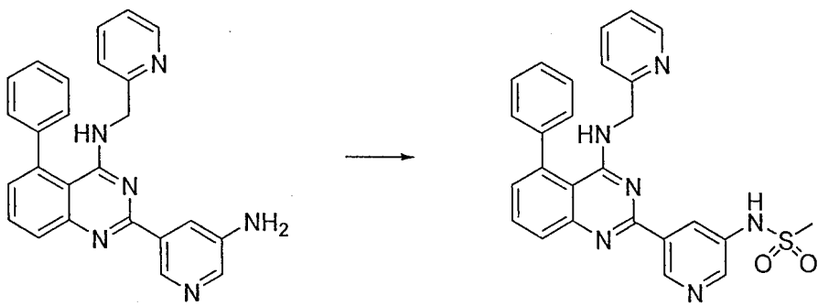


A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,20 g, 0,57 mmol) en 1,4-dioxano (5 ml) y H_2O (0,55 ml) en nitrógeno se añadió 2-amino-5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-sulfonamida (0,259, 0,800 mmol), y carbonato potásico (0,239 g, 1,70 mmol). Tras finalizar la adición, la mezcla de reacción se desgasificó con nitrógeno durante 15 minutos. Después de este periodo se añadió el complejo cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (0,023 mg, 0,020 mmol) y la mezcla resultante se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se calentó hasta 90ºC, temperatura a la cual se agitó durante 16 horas. Al finalizar este periodo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente. Una vez a la temperatura prescrita, la mezcla de reacción se inactivó mediante la adición de agua. La mezcla de reacción se transfirió a un embudo de separación y la capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El concentrado resultante se purificó mediante cromatografía en columna en gel de sílice usando una

mezcla de diclorometano/metanol como eluyente y se purificó después mediante HPLC preparativa usando 7% de metanol en diclorometano como eluyente, dando el Ejemplo 168 (0,060 g, rendimiento del 22%) en forma de un sólido blancuzco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,14 (d, 1H, J = 2,4Hz); 9,02 (d, 1H, J = 2,4Hz); 8,37 (d, 1H, J = 3,6Hz); 7,87 (dd, 1H, J = 1,2, 8,4Hz): 7,82-7,72 (m, 2H); 7,58-7,47 (a s, 5H), 7,35-7,23 (m, 3H); 4,71 (s, 2H). CLEM Procedimiento Y: tiempo de retención 1,87 min, [M+1] = 484,2; HPLC Procedimiento A2: Pureza del 98,1 %, tiempo de retención = 12,93 minutos. HPLC preparativa Procedimiento-I.

EJEMPLO 169

N-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)metano-sulfonamida



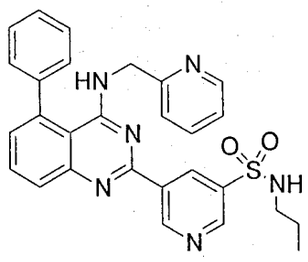
A una solución agitada de 2-(5-aminopirimidin-3-il)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (Ejemplo 161: 0,12 g, 0,3 mmol) y TEA (0,080 ml, 0,45 mmol) en DCM (10 ml) a temperatura ambiente se añadió cloruro de metanosulfonilo (0,30 ml, 0,44 mmol) gota a gota a 01C y la mezcla de reacción se agitó a temperatura ambiente durante 2 horas. La mezcla de reacción se diluyó con agua y la solución resultante se extrajo con DCM. Los extractos orgánicos combinados se lavaron sucesivamente con agua y

salmuera, se secaron, se filtraron y el filtrado se concentró. El residuo se purificó mediante cromatografía en columna en gel de sílice usando una mezcla de diclorometano/metanol (98/2) como eluyente, proporcionando el Ejemplo 169 (65 mg, rendimiento del 45 %) en forma de un sólido blancuzco. RMN ^{1}H (400 MHz, DMSO-d_6) δ: 10,35 (as, 1H); 9,40 (s, 1H); 8,68 (s, 1H), 8,58 (s, 1H), 7,24 (d, 1H, J = 3,2Hz), 7,90-7,82 (m, 2H), 7,73 (dd, 1H, J = 1,2Hz, 7,2Hz), 7,62-7,50 (m, 5H), 7,34-7,30 (m, 2H), 7,23 (t, 1H, J = 5,2Hz), 6,85 (t, 1H, J = 4Hz), 4,73 (d, 2H, J = 4Hz), 3,11 (s, 3H). CLEM Procedimiento Y: tiempo de retención 1,89 min, [M+1] = 483,2

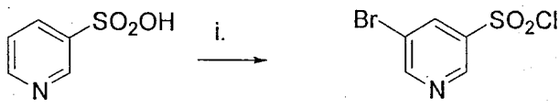
HPLC Procedimiento A1: pureza 97,8%, tiempo de retención = 6,61 min.

EJEMPLO 170

N-(2-metoxietil)-5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-sulfonamida



Etapa 1. Preparación de cloruro de 5-bromopiridin-3-sulfonilo.



Una mezcla de ácido piridin-3-sulfónico (10,3 g, 64,8 mmol),

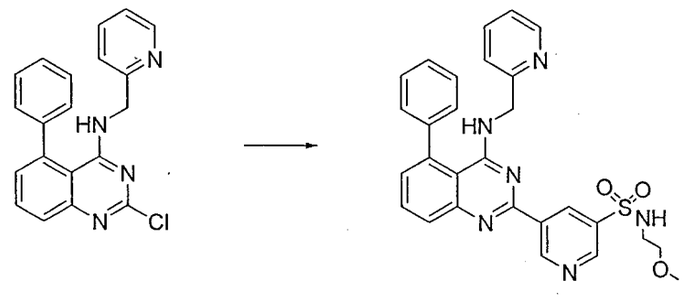
pentacloruro de fósforo (208 g, 100 mmol) y oxicloruro de fósforo (10 ml, 100 mmol) se calentó a reflujo durante 4 horas. La mezcla de reacción se dejó enfriar hasta la temperatura ambiente y se evaporó hasta sequedad a presión reducida. El residuo se trató con bromo (6,00 ml, 116 mmol) y se calentó a reflujo durante 14 horas. La mezcla de reacción se enfrió hasta 0ºC, después se inactivó lentamente mediante la adición de agua helada. La mezcla resultante se diluyó con acetato de etilo, la capa orgánica se separó y la capa acuosa se extrajo con acetato de etilo adicional. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, después se concentraron dando cloruro de 5-bromopiridin-2-sulfonilo (5,0 g) en forma de un semisólido que se usó sin purificación adicional.

Etapa 2. Preparación de 5-bromo-N-(2-metoxietil)piridin-2-sulfonamida



Una solución de cloruro de 5-bromopiridin-3-sulfonilo (1,5 g, 5,8 mmol) y 2-metoxietanamina (1,3 g, 18 mmol) en THF (40 ml) se agitó a temperatura ambiente durante 16 horas. Después de este tiempo, la mezcla de reacción resultante se repartió entre cloruro sódico acuoso saturado y acetato de etilo. La solución orgánica se secó y se evaporó. El residuo resultante se purificó mediante cromatografía en columna ultrarrápida usando acetato de etilo/hexanos dando 5-bromo-N-(2-metoxietil)piridin-3-sulfonamida (460 mg, 27%). CLEM Procedimiento T: tiempo de retención 1,13 min [M+1] = 295, 297.

Etapa 3. Ejemplo 170

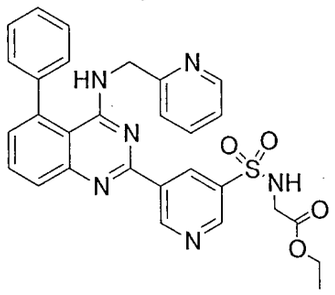


Una solución agitada de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,15 g, 0,43 mmol) en dioxano (10 ml) se desgasificó durante 10 minutos con argón y se añadieron Pd(TRIFENILFOSFINA)$_4$ (0,05 g, 0,043 mmol) y hexametildiestaño (0,25 g, 0,77 mmol) y la mezcla de reacción se agitó a temperatura ambiente durante 16 horas. A la mezcla de reacción se añadió 5-bromo-N-(2-metoxietil)piridin-3-sulfonamida (0,19 g, 0,65 mmol) y la solución resultante se calentó a 100ºC durante 16 horas adicionales. Se formó un precipitado y los sólidos se filtraron de la mezcla de reacción y el filtrado se concentró y purificó mediante cromatografía en columna en gel de sílice usando una mezcla de diclorometano/metanol como eluyente, dando el ejemplo 170 (0,065 g, 27%) en forma de un sólido blancuzco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,83 (s,1H), 9,11 (s,1H), 9,06 (s,1H), 8,24 (a s,1H), 8,19 (t, 1H, J =5,6), 7,97-7,92 (m,1H), 7,88 (t, 1H, J = 4), 7,73 (t, 1H, J = 8), 7,63-7,50 (m, 5H), 7,38-7,30 (m, 2H), 7,25 (t, 1H), 6,96 (a s, 1H), 4,76 (d, 2H, J = 4,4), 3,34-3,30 (m, 2H), 3,11 (s, 3H), 3,05 (t, 2H, J = 5,6). CLEM Procedimiento T: tiempo de retención 1,61 min, [M+1] = 527; HPLC

Procedimiento A1: pureza 99,4 %, tiempo de retención = 8,17 min.

EJEMPLO 171

2-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-sulfonamido)acetato de etilo

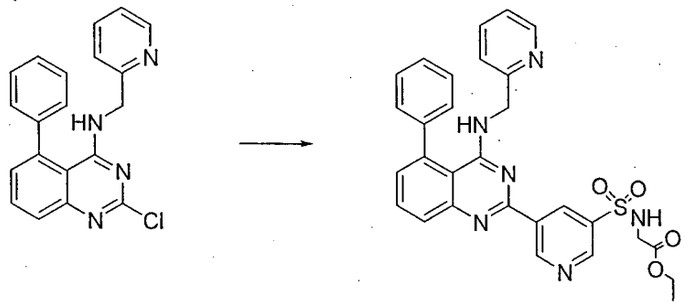


Etapa 1. Preparación de 2-(5-bromopiridin-3-sulfonamido)acetato de etilo



A una solución de cloruro de 5-bromopiridin-3-sulfonilo (3,5 g, 14 mmol) (descrito en la síntesis del Ejemplo 170) y etiléster de glicina (2,1 g, 20 mmol), diisopropiletilamina ((2,6 g, 20 mmol) en THF (70 ml) se agitó a temperatura ambiente durante 16 horas. La mezcla de reacción se repartió entre cloruro sódico acuoso saturado y acetato de etilo. La solución orgánica se separó, se secó y se evaporó a presión reducida. El residuo se purificó usando cromatografía en columna ultrarrápida usando acetato de etilo/hexanos como eluyente obteniendo 2-(5-bromopiridin-3-sulfonamido)acetato de etilo (600 mg, 14 %).. CLEM Procedimiento I: tiempo de retención 1,31 min [M+1] = 323,325.

Etapa 2. Ejemplo 171

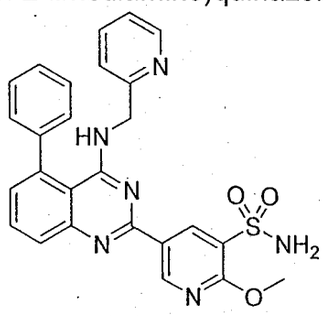


A una solución de 2-(5-bromopiridin-3-sulfonamido)acetato de metiletilo (0,20 g, 0,62 mmol) en dioxano (10 ml) se añadió hexametildiestaño (0,30 g, 0,92 mmol) y LiCl (26 mg, 0,62 mmol). La mezcla de reacción se desgasificó con nitrógeno durante 10 minutos y después se cargó con tetraquis(trifenilfosfina)paladio (68 mg, 0,061 mmol). La mezcla de reacción se agitó durante 5 horas a temperatura ambiente en atmósfera de nitrógeno. Después de este tiempo, gota a gota se añadió 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,17 g, 0,50 mmol) en dioxano (2 ml) y la mezcla de reacción se calentó hasta reflujo durante 18 horas. La mezcla de reacción se inactivó mediante la adición de agua y se extrajo con acetato de etilo. Los extractos orgánicos combinados se lavaron sucesivamente con agua y salmuera, se secaron, se filtraron y se concentraron a presión reducida. El residuo resultante se purificó mediante cromatografía en columna ultrarrápida en gel de sílice usando metanol al 5% en diclorometano, dando el Ejemplo 171 (35mg, 11%) en forma de un sólido blancuzco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,82 (s, 1H); 9,10 (s, 1H); 9,06 (s, 1H); 8,68 (t, 1H, J = 6,0Hz); 8,24 (d, 1H, J = 4,8Hz); 7,94 (dd, 1H, J = 1,2, 8,0Hz); 7,86 (t, 1H, 5,6Hz); 7,73 (dt, 1H, J = 1,6, 8,0Hz); 7,62-7,50 (m, 5H); 7,33-7,36 (m, 2H); 7,26-7,23 (m, 1H); 6,96 (s, 1H); 4,76 (d, 2H, J = 4Hz); 3,93 (c, 2H, J = 7,2Hz);

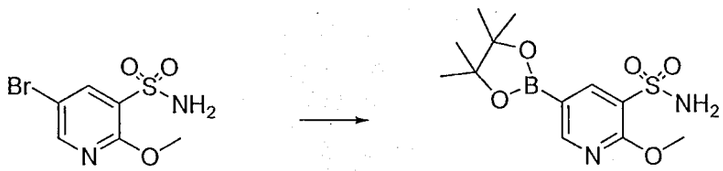
3,89 (d, 2H, *J* = 6,0Hz); 1,04 (t, 3H, *J* = 7,2Hz). CLEM Procedimiento U: tiempo de retención 1,65 min, [M+1] = 555,2; HPLC Procedimiento A4: pureza 98,9%, tiempo de retención = 9,15 min.

EJEMPLO 172

2-metoxi-5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-sulfonamida



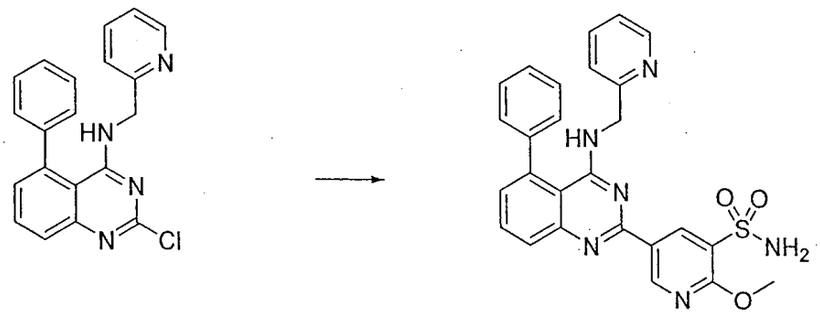
Etapa 1. Preparación de 2-metoxi-5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-piridin-3-sulfonamida



Una mezcla de 5-bromo-2-metoxipiridin-3-sulfonamida (descrita en la síntesis del Ejemplo 167: (0,15 g, 0,56 mmol), bis(pinacolato)diboro (0,17 g, 0,6 mmol) y acetato potásico (0,22 g, 2,2 mmol) en 1,4-dioxano (10 ml) se desgasificó con nitrógeno durante 15 minutos. Después de este tiempo se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio(II) diclorometano (0,036 g, 0,04 mmol) y la mezcla se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se calentó en el microondas a 120ºC durante 45 minutos. La mezcla de reacción se filtró a

través de celite y el filtrado se concentró a presión reducida proporcionando 2-metoxi-5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-sulfonamida (0,15 g), que se usó sin purificación adicional. CLEM Procedimiento T: tiempo de retención 0,44 min [M+1] = 233,0.

Etapa 2. Ejemplo 172



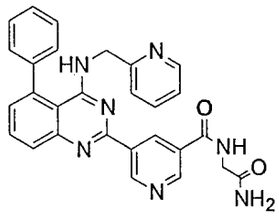
A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,19 g, 0,5 mmol) en 1,4-dioxano (5 ml) y H_2O (0,55 ml) en nitrógeno se añadió 2-metoxi-5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-sulfonamida (0,15 g, 0,60 mmol), y carbonato potásico (0,22 g, 1,6 mmol). La mezcla de reacción se desgasificó con nitrógeno durante 15 minutos. Se añadió el complejo cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (0,22 mg, 0,02 mmol) y la mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se AGITÓ A 90ºC durante 16 horas, después se dejó enfriar hasta la temperatura ambiente y se inactivó mediante la adición de agua. La mezcla de reacción se transfirió a un embudo de separación y la capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se

concentraron a presión reducida. El concentrado se purificó mediante cromatografía en columna dando el Ejemplo 172 (0,060 g, rendimiento del 22%). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 12,78 (a s, 1H); 9,03 (d, 1H, *J* = 2Hz); 8,66 (s, 1H); 8,24 (d, 1H, *J* = 4,8Hz); 7,86-7,75 (m, 2H); 7,71 (t, 1H, *J* = 7,6Hz); 7,60-7,46 (m, 5H); 7,30-7,20 (m, 3H); 7,07 (a s, 2H); 6,80 (a s, 1H); 4,67 (d, 2H, *J* = 4Hz). CLEM Procedimiento U: tiempo de retención 1,32 min [M+1] = 485,0;

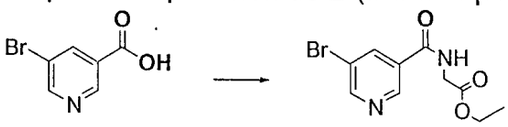
HPLC Procedimiento A4: pureza 97,1 %, tiempo de retención = 5,91 min.

EJEMPLO 173

N-(2-amino-2-oxoetil)-5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)nicotinamida



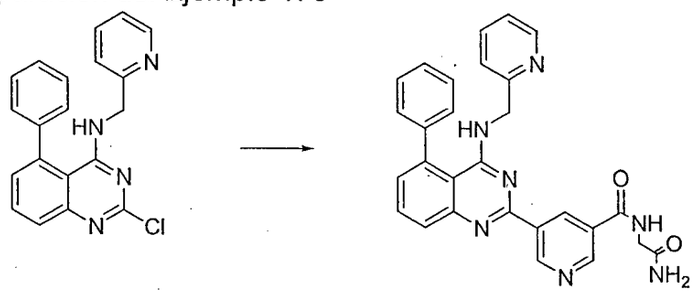
Etapa 1. Preparación de 2-(5-bromopiridinnicotinamido)acetato de etilo



Una solución de ácido 5-bromonicotínico (4 g, 0,02 mol) en cloruro de tionilo (25 ml) se calentó a reflujo durante 4 horas. El exceso de cloruro de tionilo se eliminó a presión reducida proporcionando cloruro de 5-brononicotinilo, que se usó sin purificación adicional. A cloruro de 5-brononicotinilo (3,5 g, 13,6 mmol) se añadió etiléster de glicina (2,1 g, 20,3

mmol) y diisopropiletilamina (2,6 g, 20,1 mmol) en THF (70 ml) y la mezcla de reacción se agitó a temperatura ambiente durante 16 horas. La mezcla de reacción se diluyó con EtOAc y se lavó con solución de salmuera. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida, y el residuo se purificó mediante cromatografía en columna en gel de sílice usando EtOAc 25% en hexano, proporcionando 2-(5-bromonicotinamido)acetato de etilo 1,2 g (33%) en forma de un sólido marrón. CLEM Procedimiento T: tiempo de retención 1,28 min [M+1] = 288,2;

Etapa 2. Preparación del Ejemplo 173

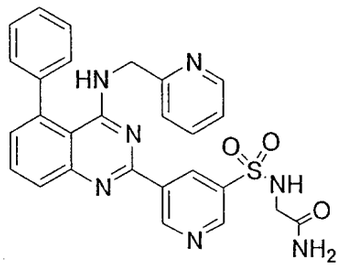


A una solución de N-(2-amino-2-oxoetil)-5-bromonicotinamida (0,220 g, 0,852 mmol) en dioxano (4 ml) se añadió hexametildiestaño (0,50 g, 1,53 mmol). La mezcla de reacción se desgasificó con nitrógeno durante 15 minutos. Se añadió Pd(trifenilfosfina)$_4$ (0,098 g, 0,08 mmol) y la mezcla de reacción se agitó a temperatura ambiente durante 6 horas. Se añadió 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,29 g 0,84 mmol) en 1,4-dioxano (3 ml) y la mezcla resultante se agitó a 95°C durante 16 horas, se dejó enfriar hasta temperatura ambiente y después se inactivó mediante la

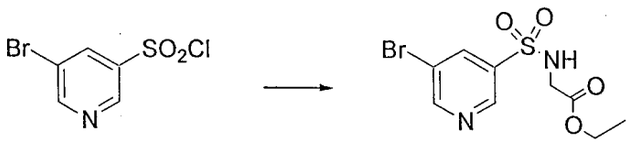
adición de agua. La mezcla de reacción se transfirió a un embudo de separación y la capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El concentrado resultante se purificó mediante cromatografía en columna en gel de sílice usando una mezcla de diclorometano/metanol como eluyente, dando el Ejemplo 173 (12 mg, 4 %) en forma de un sólido blancuzco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,76 9s, 1H); 9,21 (s, 1H); 9,16 (s, 1H); 9,14-9,11 (m, 1H); 8,24 (d, 1H, J = 4,4 Hz); 7,94 (d, 1H, J = 4,4 Hz); 7,86 (t, 1H, J = 7,6 Hz): 7,73 (dd, 1H, J = 7,6, 15,2Hz); 7,68-7,47 (m, 5H); 7,39-7,30 (m, 2H); 7,24 (dd, 1H, J = 5,2, 7,6 Hz); 7,10 (a s, 1H); 6,93 (a s, 1H); 4,77 (d, 2H, J = 4 Hz); 3,90 (d, 2H, J = 5,6 Hz). CLEM Procedimiento Y: tiempo de retención 1,70 min, [M+1] = 490,2; HPLC Procedimiento A1: pureza 99,5%, tiempo de retención = 5,73 min.

EJEMPLO 174

2-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-sulfonamido)acetamida

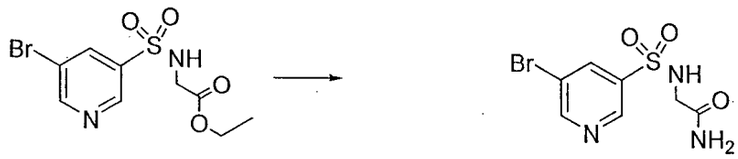


Etapa 1. Preparación de 2-(5-bromopiridin-3-sulfonamido)acetato de etilo



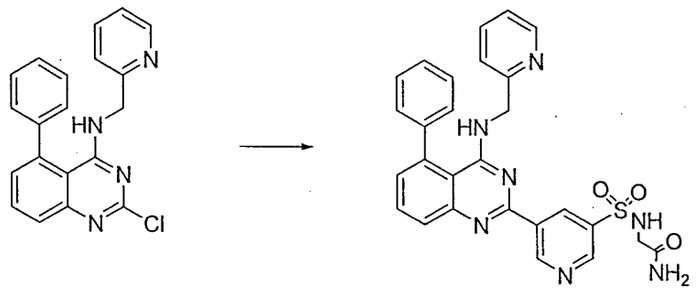
A una solución de cloruro de 5-bromopiridin-3-sulfonilo (3,5 g, 14 mmol) y etiléster de glicina (2,1 g, 20 mmol), diisopropiletilamina ((2,6 g, 20 mmol) en THF (70 ml) se agitó a temperatura ambiente durante 16 horas. La mezcla de reacción se repartió entre cloruro sódico acuoso saturado y acetato de etilo. La solución orgánica se separó, se secó y se evaporó a presión reducida. El residuo se purificó usando cromatografía en columna ultrarrápida en gel de sílice usando acetato de etilo/hexanos obteniendo 2-(5-bromopiridin-3-sulfonamido)acetato de etilo (600 mg, 14 %); CLEM Procedimiento T: tiempo de retención 1,31 min [M+1] = 323,325.

Etapa 2. Preparación de 2-(5-bromopiridin-3-sulfonamido)acetamida



Una solución de 2-(5-bromopiridin-3-sulfonamido)acetato de etilo (0,50 g, 1,7 mmol) y amoniaco en metanol (2M, 10 ml) se calentó hasta 60ºC en un tubo sellado durante 4 horas. La mezcla de reacción enfriada se concentró a presión reducida, dando 2-(5-bromopiridin-3-sulfonamido)acetamida (300 mg, 66 %), que se usó sin purificación adicional. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,96 (d, 1H, J = 2,4 Hz); 8,90 (d, 1H, J = 2 Hz); 8,39 (t, 1H, J =2 Hz), 8,21 (a s, 1H), 7,35 (a s, 1H), 7,07 (a s, 1H), 3,5 (s,2H). CLEM Procedimiento D: tiempo de retención 0,945 min [M+1] = 294.296,0.

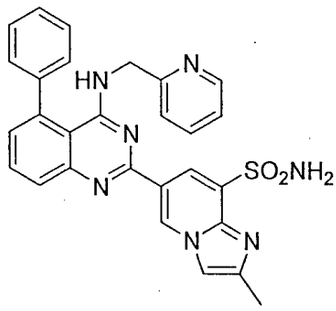
Etapa 3. Ejemplo 174



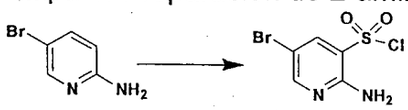
Una solución agitada de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,20 g, 0,57 mmol) en dioxano (10 ml) se desgasificó durante 10 minutos con argón y se añadieron Pd(TRIFENILFOSFINO)$_4$ (0,06 g, 0,05 mmol) y hexametildiestaño (0,34 g, 1,03 mmol) y la mezcla de reacción resultante se agitó a temperatura ambiente durante 16 horas. A la mezcla de reacción anterior se añadió 2-(5-bromopiridin-3-sulfonamida)acetamida (0,25 g, 0,86 mmol) y la solución se calentó a 100ºC durante 16 horas adicionales. Se formó un precipitado y los sólidos se filtraron de la mezcla de reacción y el filtrado se concentró y purificó mediante cromatografía en columna dando el ejemplo 174 (0,060 g, 20 %) en forma de un sólido marrón. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,80 (s, 1H), 9,11 (s, 1H), 9,05 (s, 1H), 8,25 (d, 1H, J = 4,8 Hz), 7,95 (dd, 1H, J =1,2 Hz, J =8,4 Hz), 7,86 (t, 1H, J = 8,8 Hz),7,73 (t, 1H, J = 4,4 Hz), 7,61-7,50 (m, 5H), 7,40-7,32 (m, 3H), 7,26-7,24 (m, 1H), 7,07 (a s, 1H), 6,97 (a t, 1H, J = 3,6 Hz), 4,76 (d, 2H, J = 4 Hz), 3,56 (s, 2H). CLEM Procedimiento Y: tiempo de retención 1,77 min, [M+1] = 526,0; HPLC Procedimiento A1: pureza 99,2%, tiempo de retención = 6,709 min.

EJEMPLO 175

2-metil-6-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)imidazo[1,2-a]piridin-8-sulfonamida

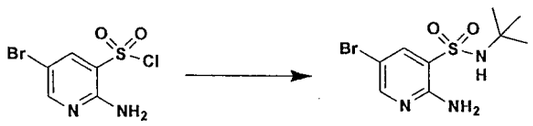


Etapa 1. Preparación de 2-amino-5-bromopiridin-3-sulfonilo



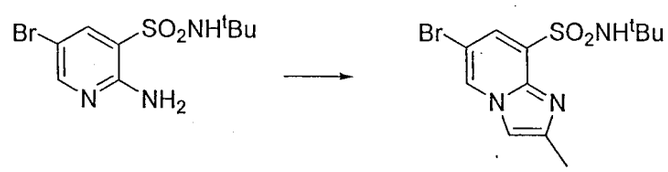
A una solución enfriada (0ºC) de ácido clorosulfónico (58 ml) en agitación enérgica se añadió 5-bromo-2-piridinamina (86,7 mmol) en porciones. Después, la mezcla de reacción se calentó a reflujo durante 3 horas. Tras enfriar hasta la temperatura ambiente, la mezcla de reacción se vertió en hielo (100 g) con agitación enérgica. El precipitado amarillo resultante se recogió mediante filtración por succión, se lavó con agua fría y éter de petróleo, proporcionando cloruro de 2-amino-5-bromopiridin-3-sulfonilo (18 g, rendimiento del 77%) en forma de un sólido naranja-amarillo.

Etapa 2. Preparación de 2-amino-5-bromo-N-terc-butilpiridin-3-sulfonamida



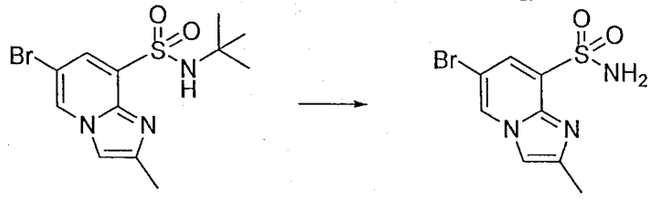
El compuesto cloruro de 2-amino-5-bromopiridin-3-sulfonilo (15 g, 55 mmol) se disolvió en THF (125 ml) y a 0ºC y se añadió t-butilamina (6,5 g, 111 mmol) y la mezcla de reacción se agitó a temperatura ambiente durante 2 horas. La mezcla de reacción se concentró a presión reducida dando 2-amino-5-bromo-N-terc-butilpiridin-3-sulfonamida (8,4 g, 49%), que se usó sin purificación adicional. CLEM Procedimiento Y: tiempo de retención 1,70 min [M+1] = 306,0

Etapa 3. Preparación de 6-bromo-N-terc-butil-2-metilimidazo[1,2-a]piridin-8-sulfonamida



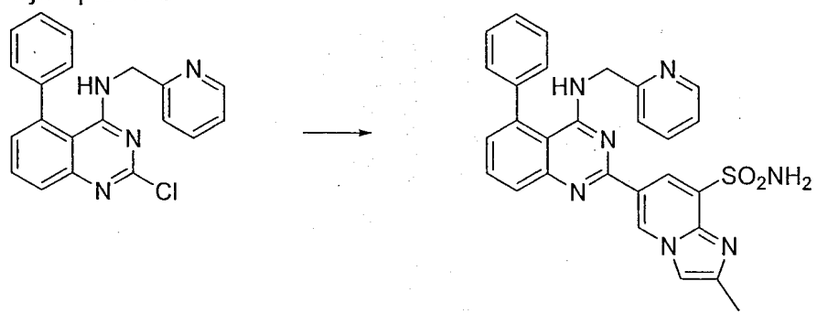
A una solución de 2-amino-5-bromo-N-terc-butilpiridin-3-sulfonamida (3,0 g, 9,7 mmol) en etanol (6 ml) se añadió cloroacetona (3,0 ml, 48 mmol) y la mezcla de reacción se agitó a 80ºC durante 48 horas. Los disolventes se evaporaron a presión reducida y el residuo se purificó mediante cromatografía en columna en gel de sílice ultrarrápida (5% de metanol en DCM), dando 6-bromo-N-terc-butil-2-metilimidazo[1,2-a]piridin-8-sulfonamida (2,2 g, 66 %), que se usó sin purificación adicional. CLEM Procedimiento T: tiempo de retención 1,33 min [M+1] = 346,64.

Etapa 4. Preparación de 6-bromo-2-metilimidazo[1,2-a]piridin-8-sulfonamida



El compuesto 6-bromo-N-terc-butil-2-metilimidazo [1, 2-a]piridin-8-sulfonamida (1,0 g, 2,8 mmol) se agitó en Tfa (6 ml) durante 16 horas. El TFA se eliminó al vacío y se añadió una solución saturada de $NaHCO_3$. La capa acuosa se extrajo con DCM, las porciones orgánicas combinadas se secaron, se filtraron y se concentraron, dando 6-bromo-2-metilimidazo[1,2-a]piridin-8-sulfonamida (0,45 g, 54 %), que se usó sin purificación adicional. CLEM Procedimiento Y: tiempo de retención 1,44 min [M+1] = 292,16.

Etapa 5. Ejemplo 175

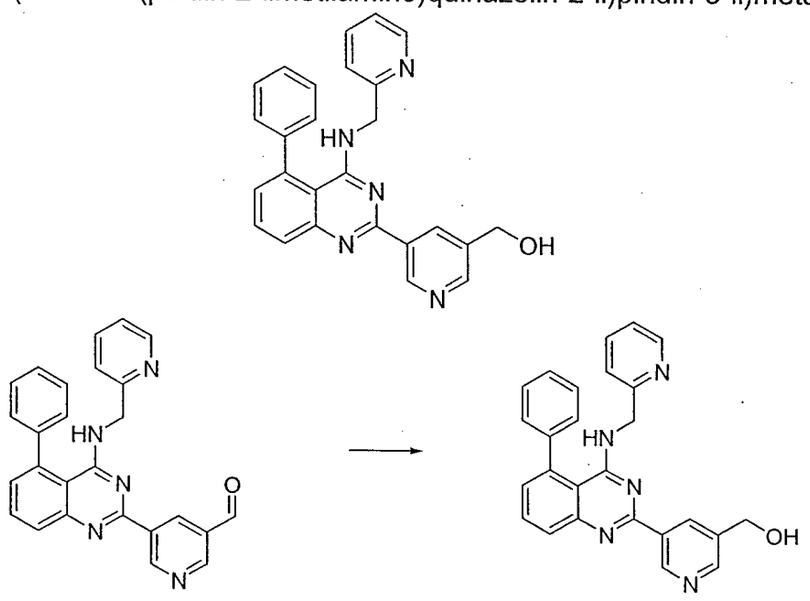


Una solución agitada de 6-bromo-2-metilimidazo[1,2-a]piridin-8-sulfonamida (0,20g, 0,68 mmol) en dioxano (10 ml) se desgasificó durante 10 minutos con argón y se añadieron $Pd(PPh_3)_4$ (0,2 g, 0,16 mmol) y hexametildiestaño (0,25 g, 1,2 mmol) y la mezcla de reacción se agitó a temperatura ambiente durante 16 horas. Se añadió 2-cloro-5-fenil-N-(piridin-2-

ilmetil)quinazolin-4-amina (0,58 g, 1,68 mmol) y la mezcla de reacción se calentó a 100ºC durante 16 horas adicionales. Se formó un precipitado y los sólidos se filtraron de la mezcla de reacción y el filtrado se concentró y purificó mediante cromatografía en columna en gel de sílice usando una mezcla de diclorometano/metanol como eluyente, obteniendo el Ejemplo 175 puro (30 mg, 10 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,73 (s, 1H); 8,77 (d, 1H, J = 1,2Hz); 8,28 (d, 1H, J = 4,4 Hz); 8,09 (s, 1H); 7,90 (d, 1H, J = 8,4 Hz); 7,84 (t, 1H, J = 6,8 Hz); 7,75 (dt, 1H, J = 6 Hz, 7,6 Hz); 7,61-7,50 (m, 6H); 7,43 (s, 1H); 7,36-7,25 (m, 3H); 6,85 (a s, 1H0; 4,78 (d, 2H, J = 4 Hz); 2,46 (s, 3H). CLEM Procedimiento X: tiempo de retención 1,59 min, [M+1] = 522,2; HPLC Procedimiento A1: pureza 98,3%, tiempo de retención = 6,63 min.

EJEMPLO 176

1-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)metanol

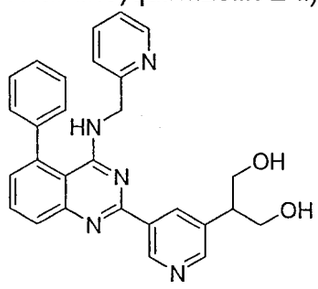


000873

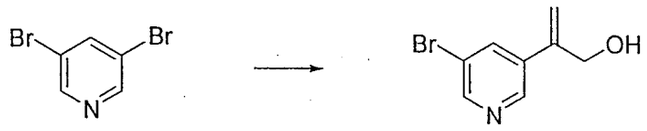
A una solución de 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il) nicotinaldehído (descrito en el Ejemplo 191, 1,0 g, 2,4 mmol) en etanol (!5 ml) se añadió $NaBH_4$ (0,28 g, 7,2 mmol). La mezcla de reacción se agitó a temperatura ambiente. Se añadió una solución saturad de cloruro amónico y la capa acuosa se extrajo con acetato de etilo. La capa orgánica se separó, se secó, se filtró y se concentró a presión reducida. El residuo resultante se purificó mediante cromatografía en columna en gel de sílice usando mezcla de diclorometano/metanol como eluyente proporcionando el Ejemplo 176 (0,71 g, rendimiento del 71 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,51 (s, 1H), 8,72 (s, 1H), 8,63 (s, 1H), 8,23 (d, 1H, J = 4,8 Hz), 7,88 (dd, 1H, J = 7,6 Hz, 8,4 Hz), 7,85 – 7,80 (m, 1H), 7,73 (dt, 1H, J = 1,2 Hz, 7,6 Hz), 7,61-7,48 (m, 5H), 7,33 (d, 2H, J =19,2 Hz), 7,27 (d, 1H, J =14 Hz), 7,23 (dt, 1H, J = 1,6, 7,2 Hz), 6,87 (t, 1H, J = 4,0 Hz, 1H), 5,47 (t, 1H, J= 5,6), 4,75 (d, 2H, J-4 Hz), 4,67 (d, 2H, J = 5,6 Hz). CLEM Procedimiento U: tiempo de retención 1,46 min, [M+1] = 420,2; HPLC Procedimiento A4: pureza 99,5%, tiempo de retención = 5,77 min.

EJEMPLO 177

2-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)propano-1,3-diol



Etapa 1. Preparación de 2-(5-bromopiridin-3-il)proa-2-en-1-ol



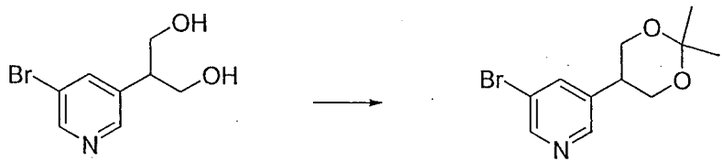
Un vial de microondas se cargó con 3,5-dibromo piridina (5,00 g, 21,1 mmol), $Pd(OAc)_2$, (0,185 g, 0,820 mmol), 1,3 – bis(difenilfosfino)propano (0,7 g 1,7 mmol) y tetrafluoroborato de 1-butil-3-metilimidazolio (25 ml) en nitrógeno a temperatura ambiente. La mezcla de reacción se desgasificó tres veces y se añadieron alcohol alílico (2,85 g, 49,1 mmol) y trietilamina (4,7 ml, 3,6 mmol). La mezcla de reacción se calentó en un reactor de microondas a 125ºC durante 2 horas. Después de enfriar hasta la temperatura ambiente se añadió HCl acuoso (20 ml, 10%) y la mezcla se agitó durante 1 hora. La mezcla de reacción se trató con Na_2CO_3 saturado (20 ml) y la porción acuosa se extrajo CH_2Cl_2. Las capas orgánicas combinadas se lavaron con agua y salmuera, se secaron con Na_2SO_4 y se evaporaron a presión reducida. El residuo resultante se purificó mediante cromatografía ultrarrápida en gel de sílice (SiO_2, hexano/EtOAc = 8/2) dando 2-(5-bromopiridin-3-il)prop-2-en-1-ol (1,6 g, 36 %). RMN ^1H (400 MHz, DMSO-d_6) δ (ppm): 8,69 (d, 1H, J = 2 Hz), 8,62 (d, 1H, J = 2,4 Hz), 8,13 (s, 1H), 5,66 (s, 1H), 5,45 (s, 1H), 5,15 (t, 1H, J = 5,2 Hz), 4,35 (d, 2H, J = 5,2 Hz). CLEM Procedimiento T: tiempo de retención 0,96 min [M+1] = 216.

Etapa 2. Preparación de 2-(5-bromopiridin-3-il)propano-1,3-diol



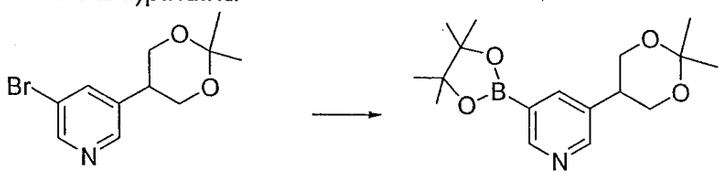
A una solución agitada de 2-(5-bromopiridin-3-il)prop-2-en-1-ol (0,600 g, 2,79 mmol) en tetrahidrofurano (5 ml) a 0 °C en nitrógeno se añadió complejo de borano-sulfuro de metilo (0,85 g, 11 mmol). La mezcla de reacción se calentó hasta 25ºC y se agitó durante 5 horas. La mezcla de reacción se enfrió hasta 0ºC y se añadió, gota a gota, hidróxido sódico (0,8 ml) 1,0N, seguido por la adición de peróxido de hidrógeno (1,0 ml, solución de 35% en peso en agua). La mezcla de reacción se agitó a 0ºC durante 2 horas, después se repartió entre acetato de etilo y agua. La capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas se combinaron, se lavaron con agua, sulfito sódico acuoso y salmuera, se secaron con Na_2SO_4, se filtraron y se concentraron a presión reducida. El compuesto 2-(5-bromopiridin-3-il)propan-1,3-diol (0,29 g, 44,7 %) se aisló mediante cromatografía en columna en gel de sílice usando EtOAc 50% en hexanos en forma de un aceite amarillo. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,53 (d, 1H, J = 2 Hz), 8,43 (d, 1H, J = 4,8 Hz), 4,92 (s, 1H), 4,69 (t, 1H, J = 4,4 Hz), 3,71-3,64 (m, 2H), 3,62-3,58 (m, 2H), 2,87 (t, J = 6,4 Hz). CLEM Procedimiento W: tiempo de retención 0,80 min [M+1] = 232.

Etapa 3. Preparación de 3-bromo-5-(2,2-dimetil-1,3-dioxan-5-il)piridina



A una solución de 2-(5-bromopiridin-3-il)propano-1,3-diol (0,12 g, 0,51 mmol) en DCM se añadió 2,2-dimetoxipropano (0,107 g, 1,03 mmol) y una cantidad catalítica de *p*-TSA. La mezcla se agitó a temperatura ambiente durante 3 horas. La mezcla de reacción se inactivó mediante la adición de solución de $NaHCO_3$ saturada y la capa orgánica se lavó sucesivamente con agua y salmuera. La capa orgánica se concentró proporcionando la 3-bromo-5(2,2-dimetil-1,3-dioxan-5-il)piridina (0,1 g, 71,4%), que se usó sin purificación adicional. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,53 (m, 2H), 8,17 (t, 2H, *J* = 2 Hz), 4,00-3,92 (m, 4H), 3,07-3,02 (m, 1H), 1,47 (s, 3H), 1,38 (s, 3H).

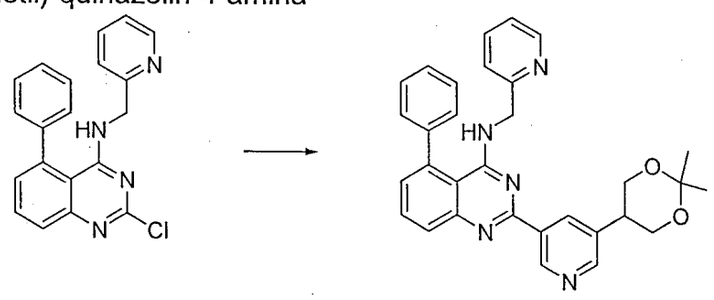
Etapa 4. Preparación de 3-(2,2-dimetil-1,3-dioxan-5-il)-5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridina



Una mezcla de 3-bromo-5-(2,2-dimetil-1,3-dioxan-5-il)piridina (0,10 g, 0,37 mmol), bis(pinacolato)diboro (0,112 g, 0,44 mmol) y acetato potásico (0,145 g, 1,40 mmol) en 1,4-dioxano (15 ml) se desgasificó con nitrógeno durante 15 minutos. Se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio(II) diclorometano (24 mg, 0,03 mmol) y la mezcla se desgasificó de nuevo durante 10 minutos con nitrógeno. La

mezcla de reacción se calentó en el reactor de microondas a 120ºC durante 45 minutos. Después de este tiempo, la mezcla de reacción se filtró a través de celite y el filtrado se concentró a presión reducida proporcionando 3-(2,2-dimetil-1,3-dioxan-5-il)-5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridina bruta (110 mg) en forma de un sólido marrón, que se usó sin purificación adicional. CLEM Procedimiento W: tiempo de retención 1,46 min [M+1] = 320,2.

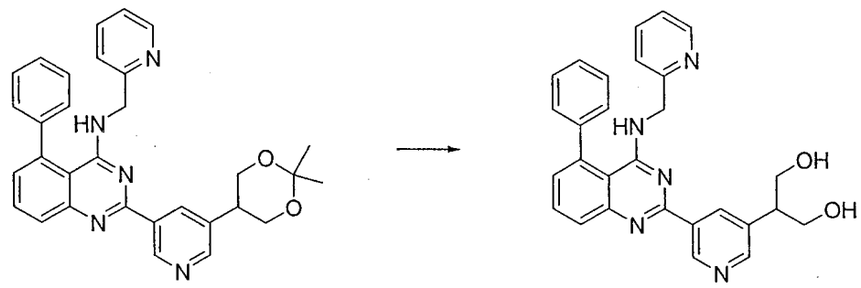
Etapa 5. Preparación de 2-(5-(2,2-dimetil-1,3-dioxan-5-il)piridin-3-il)-5-fenil-N-(piridin-2-ilmetil)-quinazolin-4-amina



A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (80 mg, 0,23 mmol) en 1,4-dioxano (6 ml) y H_2O (0,5 ml) en nitrógeno se añadió 3-(2,2-dimetil-1,3-dioxan-5-il)-5-(4,4,5,5-tetrametil-1,3,2-dioxoborolan-2-il)piridina (110 mg, 0,35 mmol), y carbonato potásico (96 mg, 7,0 mmol). La mezcla de reacción se desgasificó con nitrógeno durante 15 minutos. Se añadió el complejo cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (12 mg, 0,015 mmol) y la mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se agitó a 90ºC durante 16 horas, después se dejó enfriar hasta la temperatura

ambiente y se inactivó mediante la adición de agua. La mezcla de reacción se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El residuo resultante se purificó mediante cromatografía en columna usando EtOAc 20% en hexanos, proporcionando 2-(5-(2,2-dimetil-1,3-dioxan-5-il)piridin-3-il)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (45 mg, 39 %). CLEM Procedimiento T: tiempo de retención 1,75 min [M+1] = 504,2.

Etapa 6. Ejemplo 177

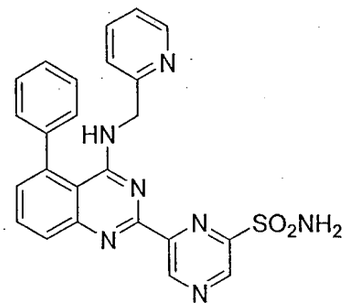


A una solución de 2-(5-(2,2-dimetil-1,3-dioxan-5-il)piridin-3-il)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (45 mg, 0,83 mmol) en metanol (5 ml) se añadió pTSA (30 mg, 0,17 mmol) y la mezcla se agitó durante 2 horas. La reacción se inactivó mediante la adición de una solución de Na_2CO_3 saturado y los disolventes volátiles se eliminaron a presión reducida. El residuo se disolvió en acetato de etilo, después se lavó con agua y salmuera. La capa orgánica se secó, se concentró y se purificó mediante filtro en columna 80% de EtOAc en hexanos, proporcionando 2-(5-(5-fenil-4-(piridin-2-

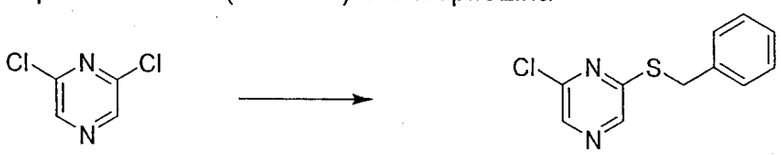
ilmetilamino)quinazolin-2-il)piridin-3-il) propano-1,3-diol (18 mg, 44 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,74 (s, 1H), 9,60 (d, 1H, J = 2 Hz), 9,56 (d, 1H, J = 2 Hz), 8,26 (d, 1H, J = 4,8 Hz), 7,90 (dd, 1H, J =1,2, 9,2 Hz), 7,83 (t, 1H, J = 7,2 Hz), 7,72 (dd, 1H, J = 1,8, 7,6 Hz), 7,61-7,50 (m, 5H), 7,38-7,30 (m, 2H), 7,26 (dt, 1H, J =1,2, 8 Hz), 6,80 (a s, 1H), 4,74 (d, 1H, J = 4,4 Hz), 4,70 (t, 1H, J = 5,2Hz), 3,85-3,77 (m, 2H), 3,76-3,68 (m, 2H), 3,30-2,95 (m, 1H). CLEM Procedimiento T: tiempo de retención 1,40 min, [M+1] = 464,2; HPLC Procedimiento A4: pureza 99,4 %, tiempo de retención = 5,48 min.

EJEMPLO 178

6-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)pirazin-2-sulfonamida



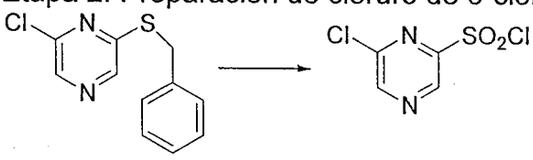
Etapa 1. Preparación de 2-(benciltio)-6-cloropirazina



A una solución agitada de 2,6-dicloropirazina (4,50 g, 30,2 mmol) y carbonato potásico (3,75 g, 27,1 mmol) en DMF (50 ml) se añadió mercaptano de bencilo (3,37 g, 27,1 mmol) en DMF (20 ml). La mezcla resultante se agitó durante 16 horas a temperatura ambiente. A la mezcla de

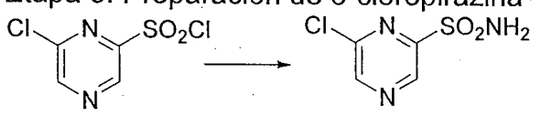
reacción se añadió agua (200 ml). La capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas se combinaron, se lavaron sucesivamente con agua, sulfito sódico acuoso y salmuera, se secaron sobre Na_2SO_4 anhidro, se filtraron y se concentraron a presión reducida, dando 2-(benciltio)-6-cloropirazina (6,5 g, 97%) en forma de un aceite amarillo, que se usó sin purificación adicional. CLEM Procedimiento E: tiempo de retención 2,058 min [M+1] = 236,6.

Etapa 2. Preparación de cloruro de 6-cloropirazin-2-sulfonilo



El compuesto 2-(benciltio)-6-cloropirazina (5,00 g, 21,2 mmol) se disolvió en una mezcla de tetracloruro de carbono y agua (200 ml/50 ml). La solución de reacción se purgó con gas cloro a 0ºC durante 30 minutos y se diluyó con DCM. La capa orgánica se secó, se filtró y se concentró a presión reducida, dando cloruro de 6-cloropirazin-2-sulfonilo en forma de un aceite marrón.

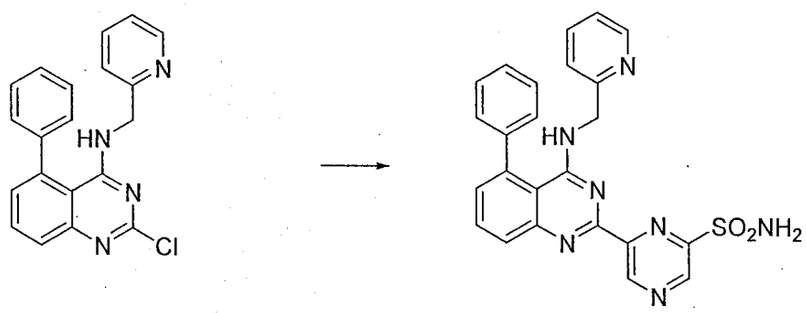
Etapa 3. Preparación de 6-cloropirazina-2-sulfonamida



El residuo cloruro de 6-clorpirazin-2-sulfonilo de la etapa 1 anterior se disolvió en THF y se purgó con gas amoniaco a -20ºC durante 15 minutos. La mezcla resultante se agitó durante 16 horas a 50ºC en un tubo sellado. El disolvente orgánico se eliminó a presión reducida y el residuo se purificó

mediante cromatografía en columna en gel de sílice usando metanol al 2,5% en diclorometano, dando 6-cloropirazin-2-sulfonamida (1,6 g, 34%) en forma de un sólido blanco. CLEM Procedimiento W: tiempo de retención 0,638 min [M+1] = 194,0.

Etapa 4. Ejemplo 178

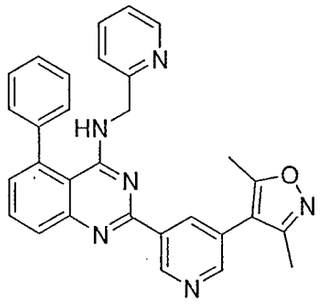


Una solución agitada de 6-clorpirazin-2-sulfonamida (0,3 g, 1,56 mmol) en dioxano (10 ml) se desgasificó durante 10 minutos con argón. Se añadieron $Pd(PPh_3)_4$ (0,17 g, 0,156 mmol) y hexametildiestaño (0,48 ml, 2,3 mmol) y la mezcla se agitó a temperatura ambiente durante 16 horas. A la mezcla de reacción se añadieron cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,43 g, 1,24 mmol) y LiCl (0,16 g, 4,68 mmol) en dioxano (2 ml) a través de una cánula y se calentó a 100ºC durante 16 horas adicionales. La mezcla de reacción se concentró a presión reducida y se añadió agua. La capa acuosa se extrajo con acetato de etilo y los extractos orgánicos se lavaron con salmuera, se secaron, se filtraron y se concentraron a presión reducida. El residuo se purificó mediante cromatografía en columna usando 20% de acetona en hexanos, después se purificó adicionalmente mediante HPLC preparativa (procedimiento H, columna: Waters SunFire 19 x 100 mm

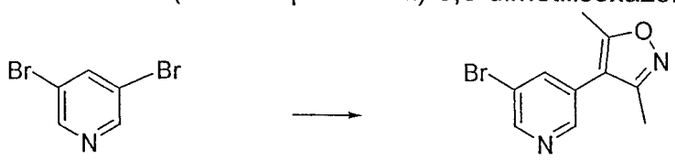
5 um C18 y TFA/agua, acetonitrilo como eluyente) proporcionando 6-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)pirazin-2-sulfonamida (35 mg, 9 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,84 (s, 1H),) 9,24 (s, 1H), 8,24 (d, 1H, J = 4,8 Hz), 7,98-7,88 (m, 4H), 7,73 (t, 1H, J = 7,6 Hz), 7,24 (t, 1H, J = 5,6 Hz), 7,00 (a s, 1H), 4,77 (d, 2H, J = 3,6 Hz). CLEM Procedimiento W: tiempo de retención 1,8 min, [M+1] = 469,0; HPLC Procedimiento A1: pureza 98,1 %, tiempo de retención = 6,74 min.

EJEMPLO 179

2-(5-(3,5-dimetilisoxazol-4-il)piridin-3-il)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina



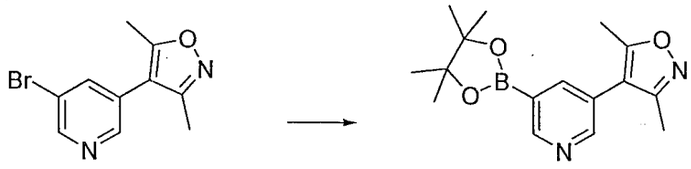
Etapa 1. Preparación de 4-(5-bromopiridin-3-il)-3,5-dimetilisoxazol



A una solución de 3.5-dibromopiridina (0,20 g, 0,85 mmol) en 1.4-dioxano (8 ml) y H_2O (0,55 ml) en nitrógeno se añadió 3,5-dimetil-4-(4,4,5,5-tetrametil-1,3;2-dioxaborolan-2-il)isoxazol (0,13 g, 0,93 mmol) y carbonato

potásico (0,,35 g, 2,5 mmol). La mezcla de reacción se desgasificó con nitrógeno durante 15 minutos. Se añadió el complejo cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (62 mg, 0,08 mmol) y la mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se agitó a 95°C durante 16 horas, después se dejó enfriar hasta la temperatura ambiente y se inactivó mediante la adición de agua. La mezcla de reacción se transfirió a un embudo de separación y la capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El residuo se purificó mediante cromatografía en columna proporcionando 4-(5-bromopiridin-3-il)-3,5-dimetilisoxazol (0,15 g, 71 %) en forma de un sólido blanco. CLEM Procedimiento T: tiempo de retención 1,52 min [M+1] = 253.

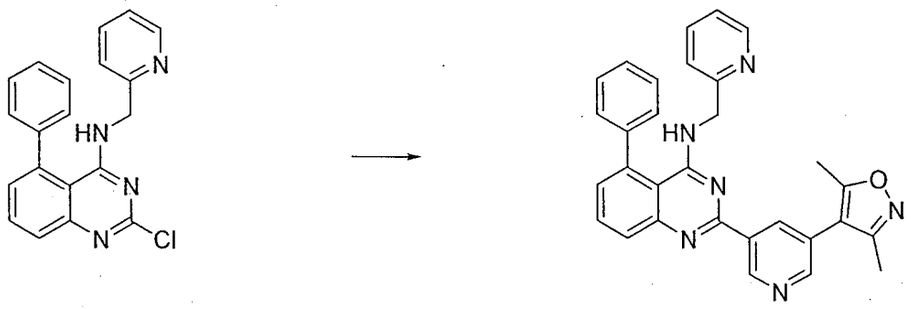
Etapa 2. Preparación de 3,5-dimetil-4-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-il)isoxazol



Una mezcla de 4-(5-bromopiridin-3-il)-3,5-dimetilisoxazol (0,16 g, 0,37 mmol), bis(pinacolato)diboro (0,24 g, 0,95 mmol) y acetato potásico (0,25 g, 1,40 mmol) en 2,4-dioxano (10 ml) se desgasificó con nitrógeno durante 15 minutos. Se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio(II) diclorometano (0,036 g, 0,05 mmol) y la mezcla se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla

de reacción se calentó en un reactor de microondas a 120ºC durante 45 minutos. La mezcla de reacción se filtró a través de celite y el filtrado se concentró a presión reducida proporcionando 3,5-metoxi-4-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-il)isoxazol (0,17 g), que se usó sin purificación adicional. CLEM Procedimiento T: tiempo de retención 0,54 min [M+1] = 219,2.

Etapa 3. Ejemplo 179



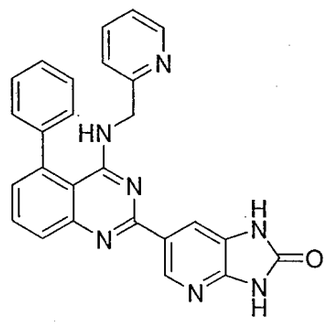
A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,,15 g, 0,43 mmol) en 1,4-dioxano (5 ml) y se añadió H_2O (0,55 ml) en nitrógeno. 3,5-dimetil-4-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-il)isoxazol (0,16 g, 0,73 mmol) y carbonato potásico (0,24 g, 1,7 mmol). La mezcla de reacción se desgasificó con nitrógeno durante 15 minutos. Se añadió el complejo cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (0,043 mg, 0,05 mmol) y la mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se agitó a 95ºC durante 16 horas, después se dejó enfriar hasta la temperatura ambiente y se inactivó con agua. La mezcla de reacción se transfirió a un embudo de separación y la capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se

secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El residuo se purificó mediante cromatografía en columna en gel de sílice usando una mezcla de diclorometano/metanol como eluyente, proporcionando el Ejemplo 179 (0,08 g, 38,2 %) en forma de un sólido blancuzco.

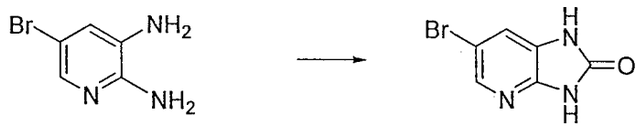
RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,72 (d, 1H, J = 4Hz), 8,70 (s, 1H), 8,60 (d, 1H, J = 2 Hz), 8,26 (d, 1H, J = 2 Hz), 7,94 (a s, 1H), 7,74 (t, 1H, J = 7,2 Hz),7,57 (dt, 1H, J = 2 Hz, 7,6 Hz), 7,52-7,48 (a s, 5H), 7,30-7,27 (m, 1H), 7,18-7,10 (m, 2H), 6,70 (a s, 1H), 4,76 (d, 2H, J = 4,0 Hz), 2,48 (s, 3H), 2,33 (s, 3H). CLEM Procedimiento T: tiempo de retención 1,82 min [M+1] = 485,2. HPLC Procedimiento A1: pureza 98,9 %, tiempo de retención = 7,67 min.

EJEMPLO 180

6-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)-1H-imidazo[4,5-b]piridin-2(3H)-ona

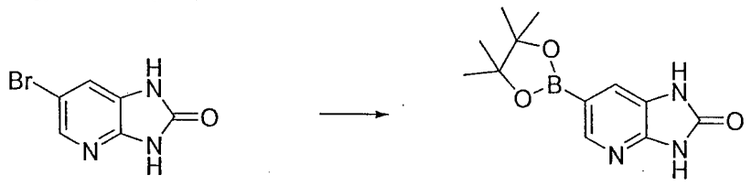


Etapa 1. Preparación de 6-bromo-1H-imidazo[4,5-b]piridin-2(3H)-ona



Una mezcla de 5-bromopiridin-2,3-diamina (2 g, 10,6 mmol) y urea (2,5 g, 41,6 mmol) se disolvió en DMF y se calentó hasta 100ºC durante 16 horas. La mezcla de reacción se diluyó con agua y se extrajo con acetato de etilo. La capa orgánica se secó sobre Na_2SO_4, después se concentró proporcionando 6-bromo-1H-imidazo[4,5-b]piridin-2(3H)-ona (0,80 g, 36 %) en forma de un sólido blancuzco, que se usó sin purificación adicional. CLEM Procedimiento W: tiempo de retención 0,98 min [M+2] = 212, 214,0.

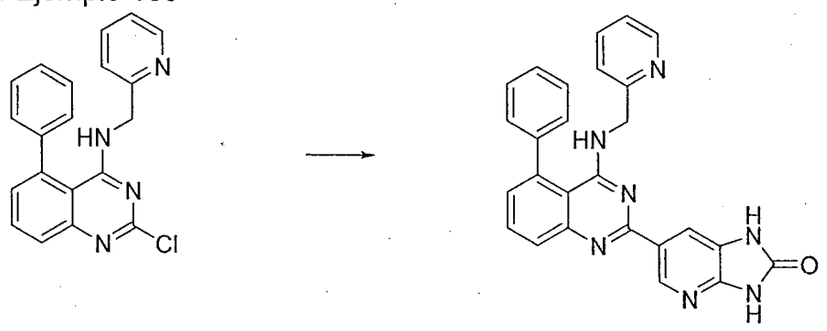
Etapa 2. Preparación de 6-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-1H-imidazo[4,5-b]piridin-2(3H)-ona



Una mezcla de 6-bromo-1H-imidazo[4,5-b]piridin-2(3H)-ona (0,500 g, 0,37 mmol), bis(pinacolato)diboro (0,895 g, 3,53 mmol) y acetato potásico (0,924 g, 1,40 mmol) en 9,42-dioxano (10 ml) se desgasificó con nitrógeno durante 15 minutos. Se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio(II) diclorometano (0,192 g, 0,23 mmol) y la mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se calentó en un reactor de microondas a 120ºC durante 45 minutos. La mezcla de reacción se filtró a través de celite y el filtrado se concentró a presión reducida proporcionando 6-(4,4,5,5-

tetrametil-1,3,2-dioxaborolan-2-il)-1H-imidazo[4,5-b]piridin-2(3H)-ona (0,3 g, 49%), que se usó sin purificación adicional. CLEM Procedimiento Y: tiempo de retención 1,5 min [M+1] = 261,7.

Etapa 3. Ejemplo 180



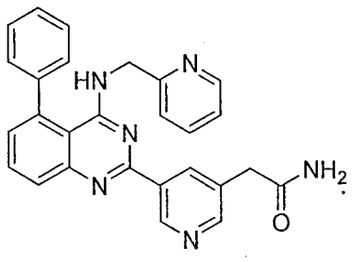
A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,0,25 g, 0,72 mmol) en 1,4-dioxano (10 ml) y se añadió H_2O (2 ml) en nitrógeno. 6-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-1H-imidazo[4,5-b]piridin-2(3H)-ona (0,28 g, 1,1 mmol) y carbonato potásico (0,2 g, 1 mmol). La mezcla de reacción se desgasificó con nitrógeno durante 15 minutos. Se añadió el complejo cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (0,06 mg, 0,07 mmol) y la mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se agitó a 90ºC durante 16 horas, después se dejó enfriar hasta la temperatura ambiente y se inactivó con agua. La mezcla de reacción se transfirió a un embudo de separación y la capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El residuo se purificó mediante cromatografía en columna en gel de sílice usando una mezcla de diclorometano/metanol como eluyente,

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proporcionando el Ejemplo 180 (0,038 g, rendimiento de I12 %) en forma de un sólido marrón. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 11,14 (a, 1H), 9,06 (s, 1H), 8,25(d, 1H, J = 4,4 Hz), 8,20 (s, 1H), 7,86-7,77 (m, 2H), 7,72 (t, 1H, J = 8 Hz), 7,60-7,49 (m, 5H), 7,31 (d, 1H, J =1,2 Hz), 7,26-7,20 (m, 2H), 6,75 (a s, 1H), 4,72 (d, 1H, J = 4,0 Hz). CLEM Procedimiento T: tiempo de retención 1,56 min, [M+1] = 446,2,0. HPLC Procedimiento A1: pureza 99,09 %, tiempo de retención = 5,83 min.

EJEMPLO 181

2-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)acetonitrilo



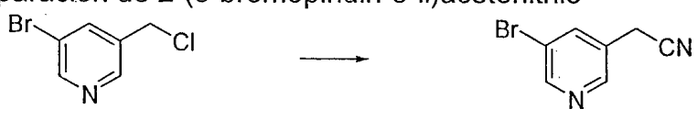
Etapa 1. Preparación de 3-bromo-5-clorometilpiridina



A una solución de (5-bromo-piridin-3-il)-metanol, (0,500 g, 2,68 mmol) en DCM (10 ml) se añadió cloruro de tionilo (0,5 ml) y la solución resultante se agitó a temperatura ambiente durante 2 horas. La mezcla de reacción se inactivó mediante la adición de agua y se extrajo en DCM. Los extractos orgánicos se lavaron con salmuera, se filtraron y se concentraron a presión

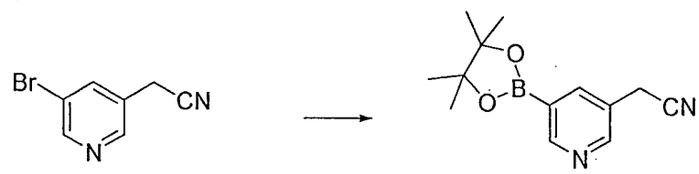
reducida proporcionando 3-bromo-5-clorometil-piridina (0,45 g, 82%), que se usó sin purificación adicional.

Etapa 2. Preparación de 2-(5-bromopiridin-3-il)acetonitrilo



El compuesto 3-bromo-5-clorometil-piridina (0,45 g; 2,2 mmol) se disolvió en DMF (10 ml). Se añadió cianuro de potasio (0,21 g, 3,27 mmol) y la mezcla de reacción se agitó a temperatura ambiente durante 16 horas. La mezcla de reacción se inactivó mediante la adición de agua y se extrajo con acetato de etilo. Las fases orgánicas se lavaron sucesivamente con agua, salmuera y se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El residuo se purificó mediante cromatografía en columna en gel de sílice usando 7% de EtOAc en hexanos, proporcionando 2-(5-bromopiridin-3-il) acetonitrilo (200 mg, 46,5 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,68 (d, 1H, J = 2 Hz), 8,51 (d, 1H, J = 2 Hz), 7,88 (t, 1H, J = 2 Hz), 3,77 (s, 2H).

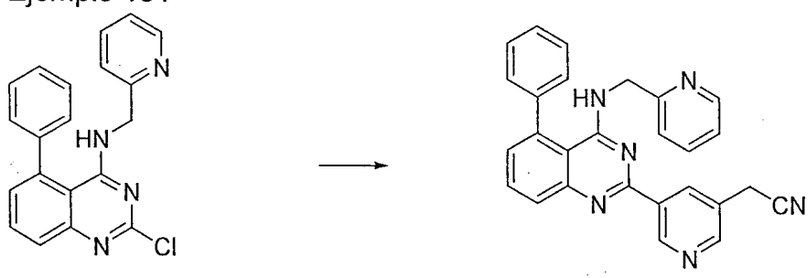
Etapa 3. Preparación de 2-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-piridin-3-il)acetonitrilo



Una mezcla de 2-(5-bromopiridin-3-il)acetonitrilo (1,5 g, 7,6 mmol), bis(pinacolato)diboro (2,9 g, 12 mmol) y acetato potásico (2,98 g, 1,40 mmol) en 1,4-dioxano (15 ml) se desgasificó con nitrógeno durante 15 minutos. Se

añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio(II) diclorometano (450 mg, 0,61 mmol) y la mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se calentó en un reactor de microondas a 95ºC durante 16 horas. La mezcla de reacción se filtró a través de celite y el filtrado se concentró a presión reducida proporcionando 2-metoxi-4-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-il)acetonitrilo (1,6 g) en forma de un sólido marrón, que se usó sin purificación adicional. CLEM Procedimiento W: tiempo de retención 1,34 min [M+1] = 245,2.

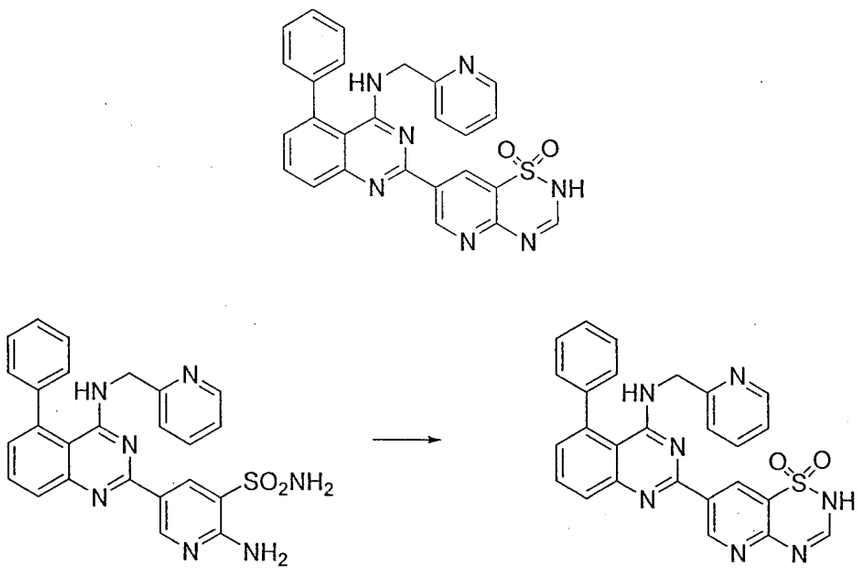
Etapa 4. Ejemplo 181



A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (180 mg, 0,52 mmol) en 1,4-dioxano (6 ml) y se añadió H_2O (0,5 ml) en nitrógeno. 2-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-il)acetonitrilo (190 mg, 0,77 mmol) y carbonato potásico (215 mg, 1,55 mmol). La mezcla de reacción se desgasificó con nitrógeno durante 15 minutos. Se añadió el complejo cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (38 mg, 0,52 mmol) y la mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se agitó a 95ºC durante 16 horas, después se dejó enfriar hasta la temperatura ambiente y se inactivó con agua. La mezcla de reacción se transfirió a un

embudo de separación y la capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El residuo se purificó mediante cromatografía en columna en gel de sílice usando metanol al 5% en diclorometano como eluyente, proporcionando el Ejemplo 181 (110 mg, 49,6 %) en forma de un sólido blancuzco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9.60 (s, 1H); 8,80 (s, 1H0; 8,70 (s, 1H); 8,24 (d, 1H, J = 4,8 Hz); 7,90 (dd, 1H, J = 1,6, 8,4 Hz); 7,84 (t, 1H, J = 7,2 Hz); 7,73 (dt, 1H, J = 1,6, 7,6 Hz); 7,62-7,50 (m, 5H); 7,36-7,30 (m, 2H); 7,23 (dd, 1H, J = 1,6, 7,2 Hz); 6,89 (t, 1H, J = 4 Hz); 4,75 (d, 2H, J = 4 Hz); 4,27 (s, 2H). CLEM Procedimiento Y: tiempo de retención 1,94 min, [M-1] = -427,0; HPLC Procedimiento A1: pureza 99,4 %, tiempo de retención = 6,95 min.

EJEMPLO 182

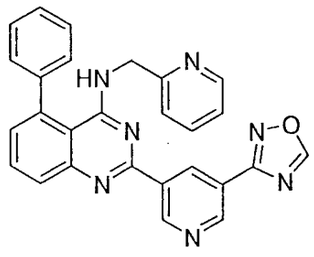


El compuesto 2-amino-5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-

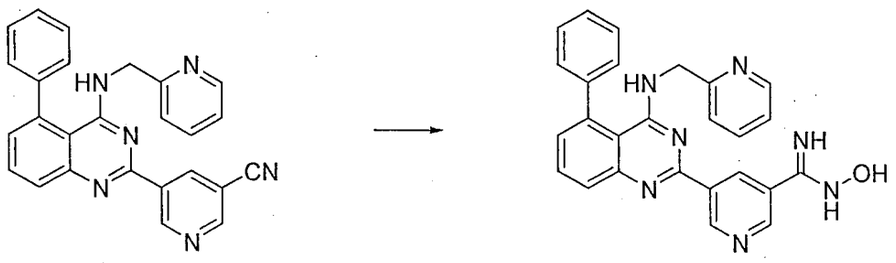
il)piridin-3-sulfonamida (Ejemplo 168, 0,095 g, 0,19 mmol) se disolvió en trimetilortoformiato (10 ml) y se sometió a reflujo a 110ºC durante 16 horas. Los disolventes volátiles se evaporaron a presión reducida y el residuo se purificó mediante cromatografía en columna en gel de sílice usando una mezcla de acetona al 30% en hexanos como eluyente, proporcionando el Ejemplo 182 (4 mg, 4%) en forma de un sólido blanco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 13,10 (a s, 1H); 9,71 (d, 1H, J = 2 Hz); 9,11 (d, 1H, J = 2 Hz); 8,24 (d, 1H, J = 4,4 Hz); 8,12 (s, 1H); 7,93 (d, 1H, J = 8,4 Hz); 7,85 (t, 1H, J = 8 Hz); 7,73 (dt, 1H, J 1,2, 8 Hz); 7,61-7,49 (m, 5H); 7,33 (dd, 2H, J = 8, 10,8 Hz); 7,23 (t, 1H, J = 8 Hz); 6,96 (a t, 1H, J = 4 Hz);4,75 (d, 2H, J = 8 Hz). CLEM Procedimiento W: tiempo de retención 1,91 min, [M+1] = 494,2; HPLC Procedimiento A4: pureza 98,0 %, tiempo de retención = 7,65 min.

EJEMPLO 183

2-(5-(1,2,4-oxadiazol-3-il)piridin-3-il)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina

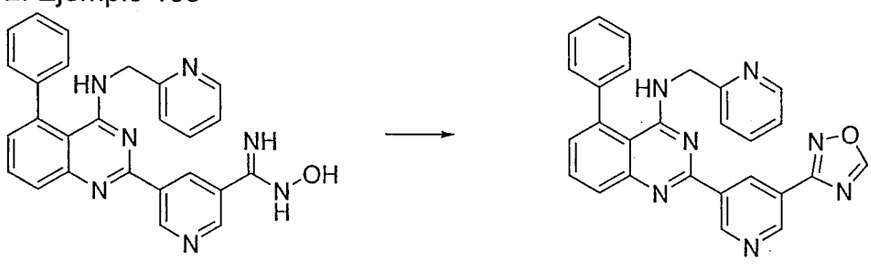


Etapa 1. Preparación de N-hidroxi-5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)nicotinimidamida



A una solución de 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il) nicotinonitrilo de etilo (descrito en el Ejemplo 6, 0,10 g, 0,24 mmol) en etanol (5 ml) se añadió clorhidrato de hidroxilamina (0,033 g, 0,48 mmol) y carbonato potásico (0,076 g, 0,72 mmol). La mezcla de reacción se calentó hasta reflujo a 80ºC durante 16 horas. El disolvente etanol se evaporó a presión reducida y el residuo se disolvió en DCM y se lavó con agua. La capa orgánica se secó, se filtró y se concentró, proporcionando N-hidroxi-5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)nicotinimidamida (0,2 g), que se usó sin purificación adicional. CLEM Procedimiento X: tiempo de retención 1,788 min [M+1] = 448,0.

Etapa 2. Ejemplo 183



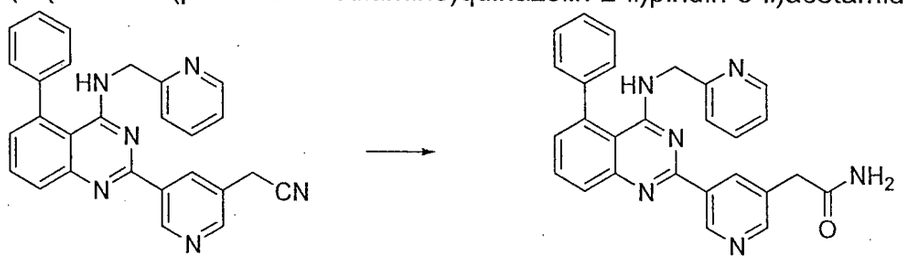
El compuesto N-hidroxi-5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)nicotinimidamida (0,10 g, 0,22 mmol) se disolvió en trimetilortoformiato (5 ml) y se añadió pTSA (cat.). La mezcla de reacción se sometió a reflujo a

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100ºC durante 16 horas. Los disolventes volátiles se evaporaron a presión reducida y el residuo se purificó mediante cromatografía en columna en gel de sílice e 1,6% de metanol en DCM, proporcionando el Ejemplo 183 (4 mg, rendimiento del 4%) en forma de un sólido blanco: RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,83 (s, 1H), 9,37-9,31 (m, 2H); 8,25 (d, 1H, J = 4 Hz); 7,96 (dd, 1H, J = 1,2, 8,4 Hz); 7,87 (dd, 1H, J = 6,8, 8,4 Hz); 7,73 (dd, 1H, J = 1,6, 7,6 Hz): 7,62-7,50 (m, 5H); 7,40-7,33 (m, 2H); 7,24 (dd, 1H, J, = 4,8, 6,8 Hz); 6,94 (as, 1H); 4,77 (d, 2H, J = 4,4 Hz). CLEM Procedimiento Y: tiempo de retención 2,03 min, [M+1] = 458,2; HPLC Procedimiento A4: pureza 94,7 %, tiempo de retención = 7,4 min.

EJEMPLO 184

2-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)acetamida

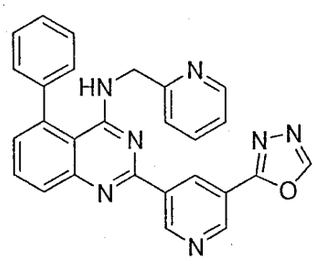


A una solución de 2-(5-(5-fenil-4-(piridin-2-ilmetilamino) quinazolin-2-il)piridin-3-il) acetonitrilo (Ejemplo 181) (70 mg, 20,1 mmol) en etanol/H_2O (3/3 ml) se añadió hidróxido sódico (40 mg, 1,0 mmol). La mezcla se calentó a reflujo durante 2 horas. La mezcla de reacción se inactivó mediante la adición de agua (5 ml) y se extrajo con acetato de etilo. Los extractos orgánicos se lavaron con salmuera saturada y se secaron sobre sulfato magnésico anhidro y se filtraron. El disolvente se evaporó a presión reducida y el residuo se purificó mediante cromatografía en columna (gel de sílice. MeOH/DCM,

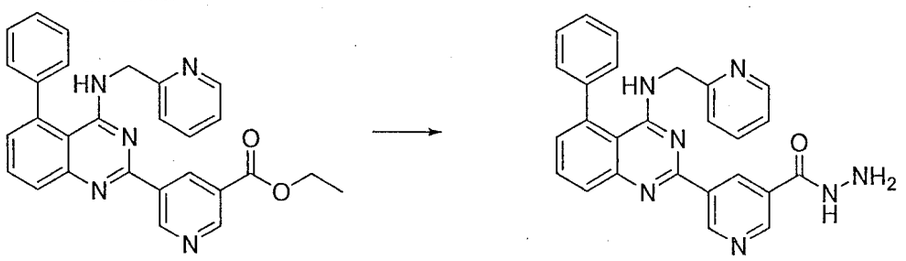
2,5:97,5) proporcionando el Ejemplo 184 (32 mg, 44 %) en forma de un sólido blancuzco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,50 (s, 1H); 8,68 (s, 1H); 8,59 (s, 1H); 8,25 (d, 1H, J = 4,4 Hz); 7,89 (dd, 1H, J = 1,2, 7,6 Hz); 7,83 (t, 1H, J = 7,2 Hz); 7,73 (dt, 1H, J = 1,6, 7,6 Hz); 7,65 (a s, 1H); 7,60-7,50 (m, 5H); 7,38-7,30 (m, 2H); 7,23 (t, 1H, J = 6,4 Hz); 7,22 (a s, 1H); 6,84 (a s, 1H); 4,75 (d, 2H, J = 4 Hz); 3,57 (s, 2H). CLEM Procedimiento Y: tiempo de retención 1,72 min, [M+1] = 447,2; HPLC Procedimiento A4: pureza 97,8 %, tiempo de retención = 5,48 min.

EJEMPLO 185

2-(5-(1,3,4-oxadiazol-2-il)piridin-3-il)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina

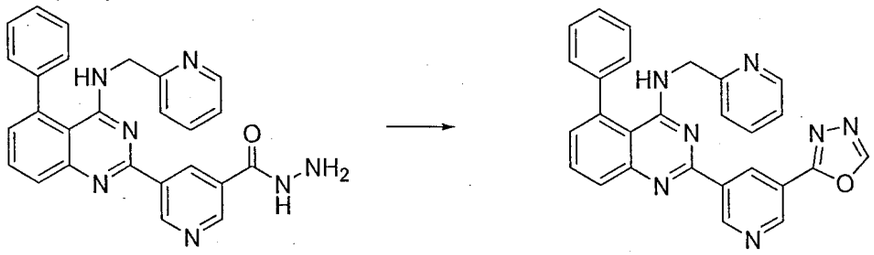


Etapa 1. Preparación de 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)nicotinohidrazida



A una solución de 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il) nicotinato de etilo (Ejemplo 43) (0,2 g, 0,43 mmol) en etanol (10 ml) se añadió hidracina hidrato (0,1 ml, 2,1 mmol). La mezcla de reacción se calentó hasta reflujo a 80ºC durante 16 horas. El etanol se evaporó a presión reducida y el residuo se disolvió en DCM y se lavó con agua. La capa orgánica se secó, se filtró y se concentró, proporcionando 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)nicotinohidrazida (0,2 g, bruto), que se usó sin purificación adicional. CLEM Procedimiento E: tiempo de retención 1,8 min [M+1] = 447,50.

Etapa 2. Ejemplo 185

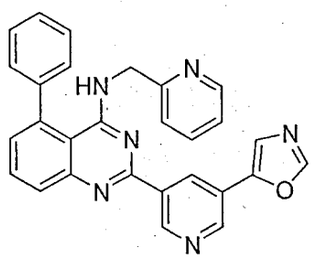


El compuesto 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)nicotinohidrazida (0,2 g, 0,44 mmol) se disolvió en trimetilortoformiato (5 ml). se añadió pTSA (catalítico) y la mezcla de reacción se calentó hasta reflujo a 110ºC durante 16 horas. Los disolventes volátiles se evaporaron a presión reducida y el residuo se purificó mediante cromatografía en columna en gel de sílice con 1,7% de metanol en DCM proporcionando el ejemplo 185 (4 mg, 2%) en forma de un sólido blanco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,86 (s, 1H), 9,53 (s, 1H); 9,33 (s, 1H); 9,31 (s, 1H); 8,25 (a s, 1H); 7,96 (dd, 1H, J = 1,2, 1,8 Hz); 7,87 (dd, 1H, J = 7,2, 8 Hz); 7,74 (dt, 1H, J = 1,8 Hz);

7,62-7,50 (m, 5H); 7,34 (dd, 2H, *J* = 7,2, 12,8 Hz); 7,25 (dd, 1H, *J* = 4,8, 6,4 Hz); 6,95 (t, 1H, *J* = 4 Hz); 4,77 (d, 2H, *J* = 4,4 Hz). CLEM Procedimiento Y: tiempo de retención 1,91 min, [M+1] = 458,2; HPLC Procedimiento A1: pureza 96,7 %, tiempo de retención = 6,85 min.

EJEMPLO 186

2-(5-oxazol-3-il)piridin-3-il)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina



Etapa 1. Preparación de 5-(5-bromopiridin-3-il)oxazol

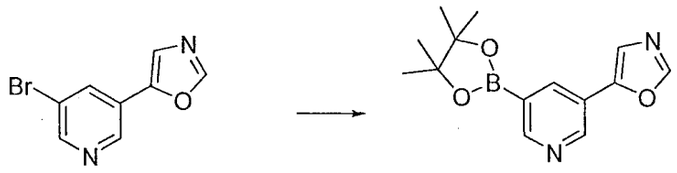


A una solución de 5-bromonicotinaldehído (0,2 g, 1 mmol) en MEOH (5 ml) se añadió K_2CO_3 (0,3 g, 2 mmol) seguido por TOSMIC (0,27 g, 1,39 mmol). La mezcla se calentó hasta 85ºC durante 2 horas. El metanol se evaporó a presión reducida y el residuo se disolvió en DCM, después se lavó con agua. Los extractos orgánicos se secaron sobre sulfato sódico, se filtraron y se concentraron. El residuo se purificó mediante cromatografía en columna en gel de sílice usando MeOH 2,1 % en DCM como eluyente,

000898

proporcionando 5-(5-bromopiridin-3-il)oxazol (0,12 g, 50 %). CLEM Procedimiento Y: tiempo de retención 1,39 min [M+1] = 225,0.

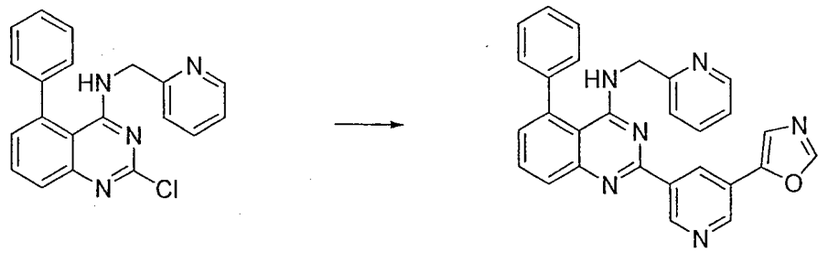
Etapa 2. Preparación de 5-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-piridin-3-il)oxazol



Una mezcla de 5-(5-bromopiridin-3-il)oxazol (0,10 g, 0,044 mmol), bis(pinacolato)diboro (0,17 g, 0,60 mmol) y acetato potásico (0,129 g, 1,3 mmol) en 1,4-dioxano (5 ml) se desgasificó con nitrógeno durante 15 minutos. Se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio(II) diclorometano (0,017 g, 0,022 mmol) y la mezcla se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se calentó en el microondas a 100ºC durante 16 horas. La mezcla de reacción se filtró a través de celite y el filtrado se concentró a presión reducida proporcionando 5-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-il)oxazol (0,1 g), que se usó sin purificación adicional.

CLEM Procedimiento W: tiempo de retención 1,45 min [M+1] = 273,2.

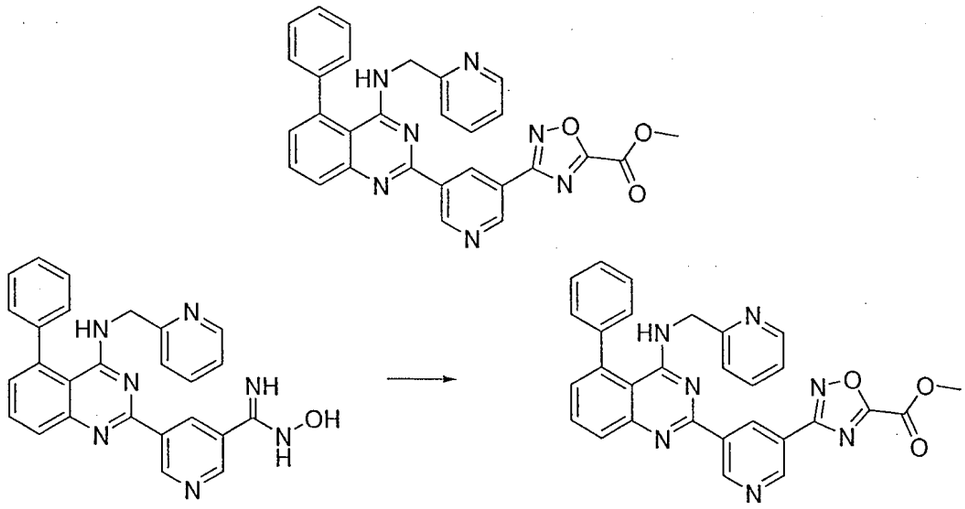
Etapa 3. Ejemplo 186



A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,115 g, 0,330 mmol) en 1,4-dioxano (6 ml) y H_2O (1,5 ml) en nitrógeno se añadió 5-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-il)oxazol (0,10 g, 0,36 mmol), y carbonato potásico (0,136 g, 0,990 mmol). La mezcla de reacción se desgasificó con nitrógeno durante 15 minutos. Se añadió el complejo cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (0,026 g, 0,033 mmol) y la mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se agitó a 100ºC durante 16 horas, después se dejó enfriar hasta la temperatura ambiente y se inactivó con agua. La mezcla de reacción se transfirió a un embudo de separación y la capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El residuo resultante se purificó mediante cromatografía en columna en gel de sílice usando metanol al 5 % en diclorometano, proporcionando 2-(5-(oxazol-5-il)piridin-3-il)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,015 g) en forma de un sólido marrón. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,70 (s, 1H); 9,03 (s, 1H); 8,27 (d, 2H, J = 3,6 Hz); 8,03 (s, 1H0; 7,77 (t, 1H, J = 7,6 Hz); 7,70-7,58 (m, 2H); 7,54-7,47 (m, 5H0; 7,33-7,28 (m, 1H); 7,20-7,10 (m, 5H0; 6,82 (a, 1h); 4,80 (d, 2H, J = 4,4 Hz). CLEM Procedimiento Y: tiempo de retención 1,98 min, [M+1] = 457,2; HPLC Procedimiento A1: pureza 98,7 %, tiempo de retención = 7,09 min.

EJEMPLO 187

3-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)-1,2,4-oxadiazol-5-carboxilato de metilo

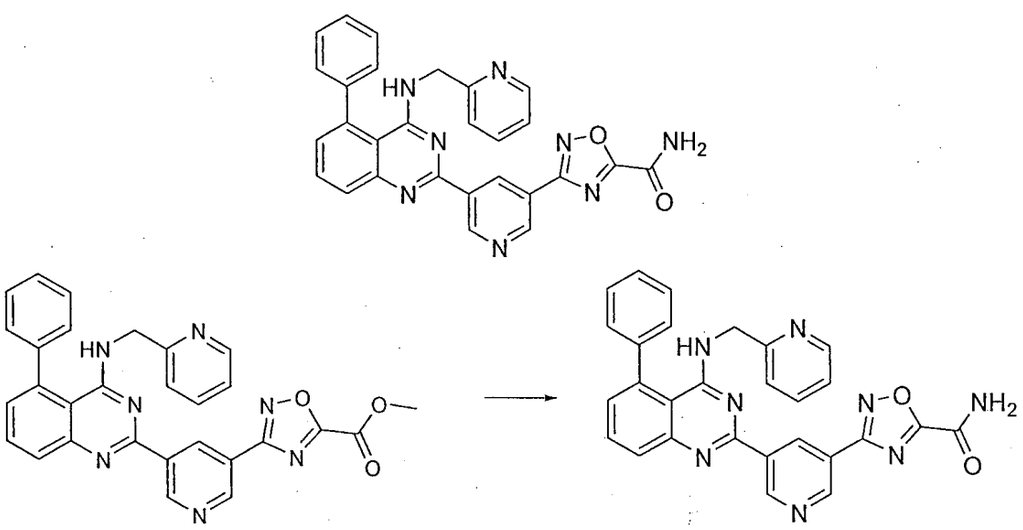


A una solución de N-hidroxi-5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il) nicotinimidamida (descrito en el Ejemplo 183, 1,0 g, 2,2 mmol) en CDE a 0ºC se añadió 2-cloro-2-oxoacetato de metilo (0,31 ml, 3,3 mmol). La mezcla de reacción se agitó a temperatura ambiente durante 2 horas. Se añadió oxicloruro de fósforo (1 ml) y la mezcla de reacción se calentó hasta reflujo durante 1,5 horas. La mezcla de reacción se inactivó mediante la adición de solución saturada de $NaHCO_3$ y se extrajo con DCM, se secó sobre sulfato sódico y se concentró. El residuo se purificó mediante cromatografía en columna en gel de sílice usando metanol al 5 % en diclorometano, proporcionando el Ejemplo 187 (270 mg, 23 %) en forma de un sólido blanco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,85 (s, 1H); 9,34 (s, 1H0; 8,27 (d, 1H, J = 5,2 Hz); 7,98 (dd, 1H, J 1,2, 8 Hz); 7,87 (t, 1H, J = 4,8 Hz); 7,76 (t, 1H, J = 3 Hz); 7,63-7,53 (m, 5H0; 7,41-7,30 (m, 2H0; 7,24 (t, 1H, J = 6 Hz); 6,95 (a s, 1H); 4,77 (d, 2H, J = 4 Hz); 4,05 (s, 3H). CLEM

Procedimiento Y: tiempo de retención 2,09 min, [M+1] = 516,2; HPLC Procedimiento A4: pureza 97,4 %, tiempo de retención = 8,77 min.

EJEMPLO 188

3-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)-1,2,4-oxadiazol-5-carboxamida



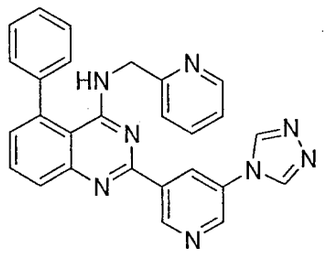
A una solución de 3-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)-1,2,4-oxadiazol-5-carboxilato de metilo (Ejemplo 187, 0,080 g, 0,15 mmol) se añadió amoniaco en metanol (10 ml) y la mezcla de reacción se calentó a 60ºC durante 4 horas. El disolvente se evaporó a presión reducida proporcionando el Ejemplo 188 (0,032 g, 45%) en forma de un sólido blanco. RMN ^{1}H (400 MHz, DMSO-d_6) δ: 9,84 (s, 1H); 9,36 (s, 1H0; 9,34 (s, 1H); 8,80 (a s, 1H); 8,35 (a s, 1H); 8,26 (d, 1H, J = 4,8 Hz); 7,98 (d, 1H, J = 8,4 Hz); 7,87 (t, 1H, J = 8 Hz); 7,74 (t, 1H, J 8 Hz); 7,63-7,50 (m, 3H);

000902

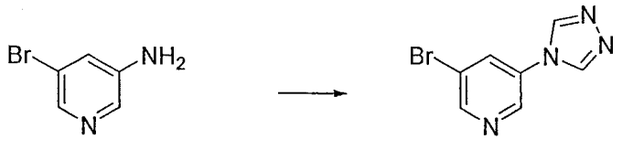
7,41-7,33 (m, 2H); 7,25 (t, 1H, *J* = 7,2 Hz); 6,96 (a t, 1H, *J* = 4 Hz); 4,78 (d, 2H, *J* = 4 Hz). CLEM Procedimiento Y: tiempo de retención 1,89 min, [M+1] = 501,2. HPLC Procedimiento A1: pureza 96,4 %, tiempo de retención = 7,05 min.

EJEMPLO 189

2-(5-(4H-1,2,4-triazol-4-il)piridin-3-il)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina



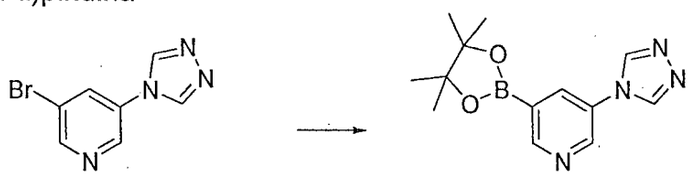
Etapa 1. Preparación de 3-bromo-5-(4H-1,2,4-triazol-4-il)piridina



Una mezcla de 3-bromo-5-amino-piridina (0,30 g, 1,7 mmol) y N,N-diformailhidracina (0,15 g, 1,7 mmol) se calentó a 150ºC en un tubo sellado durante 16 horas. Se formó un precipitado que se disolvió en etanol caliente y después se filtró. Al filtrado se añadió éter dietílico a temperatura ambiente y la suspensión espesa se agitó durante la noche. El sólido resultante se separó y se purificó mediante cromatografía en columna en gel de sílice

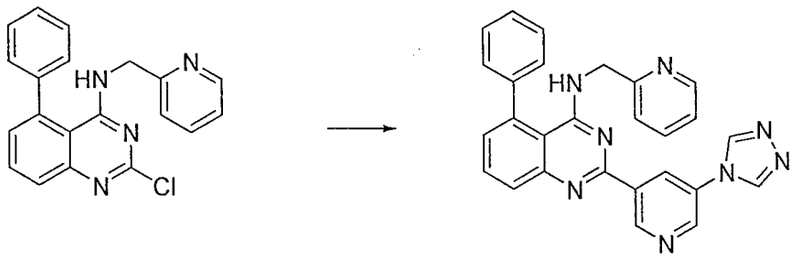
usando una mezcla de acetato de etilo y hexanos como eluyente, proporcionando 3-bromo-5-(4H-1,2,4-triazol-4-il)piridina (130 mg, rendimiento del 33%) en forma de sólido blanco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,24 (s, 2H); 9,03 (d, 1H, J = 2 Hz); 8,79 (d, 1H, J = 2 Hz); 8,60 (t, 1H, J = 2 Hz).

Etapa 2. Preparación de 3-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-5-(4H-1,2,4-triazol-4-il)piridina



Una mezcla de 3-bromo-5-(4H-1,2,4-triazol-4-il)piridina (0,12 g, 0,50 mmol), bis(pinacolato)diboro (0,16 g, 0,60 mmol) y acetato potásico (0,15 g, 1,5 mmol) en 1,4-dioxano (15 ml) se desgasificó con nitrógeno durante 15 minutos. Se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio(II) diclorometano (0,043 g, 0,05 mmol) y la mezcla resultante se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se calentó en un reactor de microondas a 120°C durante 45 minutos. Después de este tiempo, la mezcla de reacción se filtró a través de celite y el filtrado se concentró a presión reducida proporcionando 3-4-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-5-(4H-1,2,4-triazol-4-il)piridina (150 mg), que se usó sin purificación adicional.

Etapa 3. Ejemplo 189

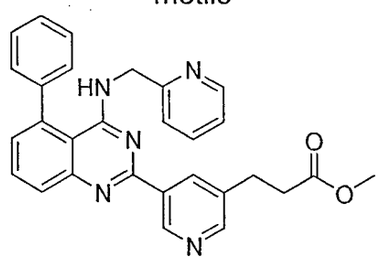


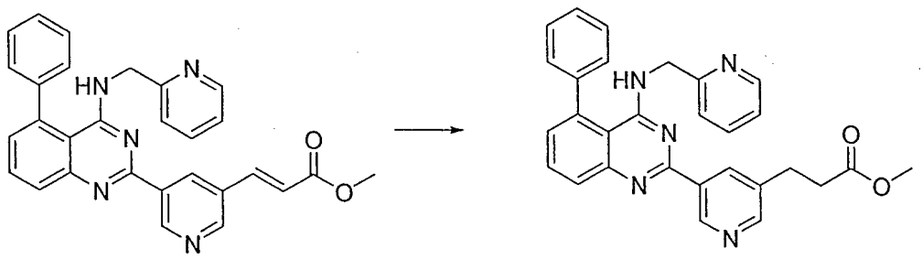
A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (180 mg, 0,5 mmol) en 1,4-dioxano (6 ml) y H_2O (1,5 ml) en nitrógeno se añadió 3-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-5-(4H-1,2,4-triazol-4-il)piridina (150 mg, 0,700 mmol), y carbonato potásico (215 mg, 1,50 mmol). Tras finalizar la adición, la mezcla se desgasificó con nitrógeno durante 15 minutos y después se añadió complejo de cloruro d (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (0,041 g, 0,050 mmol). La mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. Al finalizar este periodo, la mezcla de reacción se agitó a 90°C durante 16 horas, se dejó enfriar hasta la temperatura ambiente y después se inactivó con agua. La mezcla de reacción se transfirió a un embudo de separación y la capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El residuo resultante se purificó mediante TLC preparativa usando 5% de metanol en diclorometano dando el Ejemplo 189 (6 mg, rendimiento del 3%) en forma de un sólido marrón. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,70 (s, 1H), 9,34 (s, 2H), 9,07 (s, 1H), 8,97 (s, 1H), 8,22 (d, 1H, J = 4,4 Hz), 7,93 (dd, 1H, J = 1,2, 8,4 Hz), 7,86 (t, 1H, J = 6 Hz), 7,73 (dt, 1H, J = 1,6, 7,6 Hz), 7,50-7,62 (m, 5H); 7,36-7,32 (m, 2H); 7,23 (t, 1H, J = 5,6 Hz), 6,97 (t, 1H, J = 4 Hz), 4,79 (d,

2H, *J* = 4,0 Hz). CLEM Procedimiento Y: tiempo de retención 1,79 min, [M-1] = 455,2; HPLC Procedimiento A3: pureza 98,9 %, tiempo de retención = 13,5 min.

EJEMPLO 190

3-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)propanoato de metilo



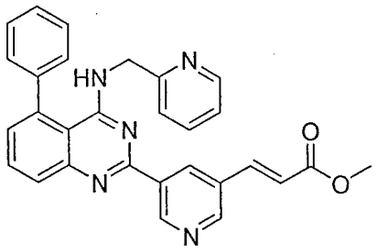


A una solución de 3-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)acrilato de (E)-metilo (Ejemplo 191, preparado de un modo similar al procedimiento descrito más adelante, 0,3 g, 6,3 mmol) en etanol (7 ml) se añadió 10% de paladio sobre carbono (100 mg). Tras finalizar la adición, la mezcla de reacción se agitó a temperatura ambiente en hidrógeno durante 16 horas. Después de este tiempo, la mezcla de reacción se filtró a través de celite y el disolvente se evaporó a presión reducida. El residuo resultante se purificó mediante cromatografía en columna en gel de sílice usando metanol

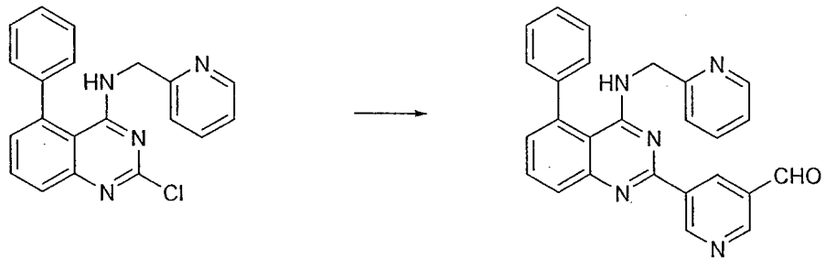
en DCM (2:98) como eluyente proporcionando el Ejemplo 190 (180 mg, rendimiento del 60 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,47 (s, 1H), 8,63-8,57 (m, 2H), 8,23 (a s, 1H), 7,87 (d, 1H, J = 6,8 Hz), 7,82 (t, 1H, J = 6,8 Hz), 7,72 (dt, 1H, J = 2, 7,6 Hz), 7,63 -7,49 (m, 5H), 7,36 -7,28 (m, 2H), 7,23 (dd, 1H, J =5,2, 6,8 Hz), 6,83 (t, 1H, J = 4,4 Hz), 4,73 (d, 2H, J = 2 Hz), 3,00 (t, 2H, J = 7,6 Hz), 2,76 (t, 2H, J = 7,6 Hz). CLEM Procedimiento W: tiempo de retención 2,17 min, [M+1] = 476,2; HPLC Procedimiento A1: pureza 98,7 %, tiempo de retención = 7,10 min.

EJEMPLO 191

3-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)acrilato de (E)-metilo

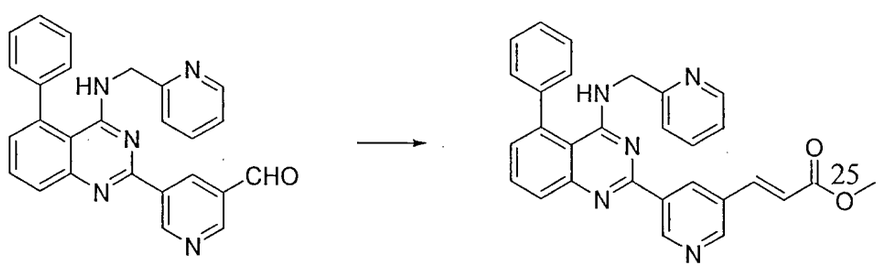


Etapa 1. Preparación de 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)nicotinaldehído



A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (2g, 5,7 mmol) en 1,4-dioxano (40 ml) y H_2O (8 ml) en nitrógeno se añadió 5-metoxi-5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)nicotinaldehído (1,48 g, 6,30 mmol), y carbonato potásico (2,39 g, 17,0 mmol). Tras la finalización de la adición, la mezcla de reacción se desgasificó con nitrógeno durante 15 minutos y, después, se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (0,46 mg, 0,050 mmol). La mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. Al finalizar este periodo, la mezcla de reacción se agitó a 90ºC durante 16 horas, después se dejó enfriar hasta la temperatura ambiente y se inactivó mediante la adición de agua. La mezcla de reacción se transfirió a un embudo de separación y la capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El concentrado resultante se purificó mediante cromatografía en columna en gel de sílice usando 2,7% de MeOH en DCM como eluyente, dando 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)nicotinaldehído (1,8 g, rendimiento del 100 %) en forma de un sólido blancuzco. CLEM Procedimiento Y: tiempo de retención 1,99 min [M+1] = 418,4.

Etapa 2. Ejemplo 191

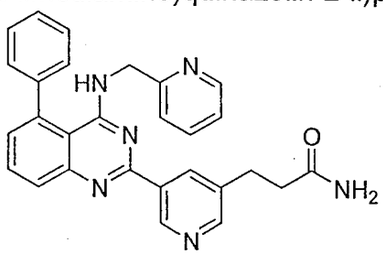


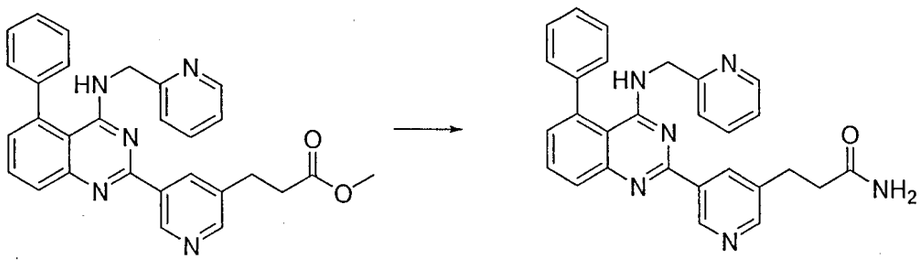
A una solución de 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il) nicotinaldehído (250 mg, 0,60 mmol) en THF (15 ml) se añadió (trifenilfosforanilidina)acetato de metilo (300 mg, 0,9 mmol). La solución resultante a temperatura ambiente durante 16 horas. Después de este tiempo, el disolvente se eliminó a presión reducida dando un residuo. El residuo resultante se purificó mediante cromatografía en columna en gel de sílice usando 20% de EtOAc, hexano como eluyente proporcionando el Ejemplo 191 (0,18 g, rendimiento del 63 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,57 (s, 1H), 8,31 (d, J= 4,8, 1H), 8,15 (d, J= 8,4 Hz, 1H), 8,04-7,89 (m, 1H), 7,92-7,84 (m, 2H), 7,63-7,55 (m, 5H),7,51-7,43 (m, 2H), 7,37 (t, J= 5,6 Hz, 1H), 7,00 (d, *J* = 16 Hz, 1H), 4,93 (d, *J* = 4 Hz, 2H), 3,79 (s, 3H). CLEM Procedimiento Y: tiempo de retención 2,15 min [M+1] = 474,1;

HPLC Procedimiento A1: pureza 99,0 %, tiempo de retención = 7,85 min.

EJEMPLO 192

3-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)propanamida

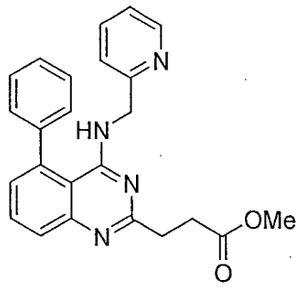




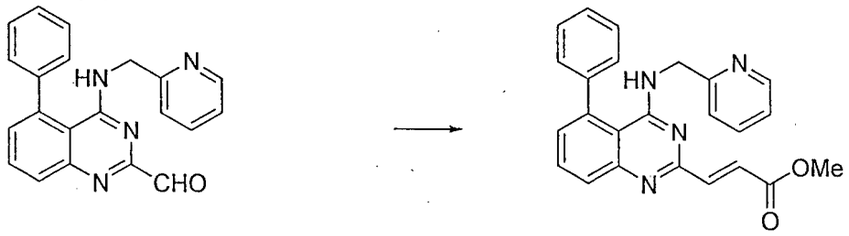
Una solución del Ejemplo 190 (0,1 g, 0,2 mmol) en NH_3 (2,0 M en MeOH, 5 ml) se agitó a temperatura ambiente en un vaso sellado durante 30 minutos. Después de este tiempo, el sólido formado se recogió mediante filtración y se lavó con metanol enfriado con hielo. El sólido se purificó después mediante cromatografía en columna en gel de sílice usando 5 % de metanol en DCM como eluyente proporcionando el Ejemplo 192 (35 mg, 35 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,45 (s, 1H); 8,55 (s, 1H); 8,24 (d, 1H, J = 4 Hz); 7,88 (dd, 1H, J = 1,2, 8,0 Hz): 7,80 (t, 1H< J = 8 Hz); 7,72 (dt, 1H, J =1,2, 8 Hz); 7,60-749 (m, 5H); 7,40-7,30 (m, 2H); 7,29 (dd, 1H, J = 1,2, 7,2 Hz); 7,23 (dd, 1H, J = 5,2, 6,8 Hz); 6,84 (t, 1H, 3,2 Hz); 4,73 (d, 2H, 4 Hz); 2,95 (t, 2H, J = 7,6 Hz); 2,48 (t, 2H, 7,6 Hz). CLEM Procedimiento W: tiempo de retención 1,64 min, [M+1] = 461,2; HPLC Procedimiento A1: pureza 99,1 %, tiempo de retención = 5,76 min.

EJEMPLO 193

3-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)propanoato de metilo



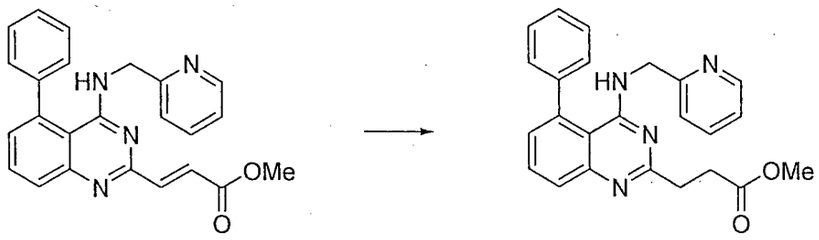
Etapa 1. Preparación de 3-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)acrilato de (E)-metilo



A una solución de fosfonoacetato de trimetilo (0,225 g, 1,00 mmol) en THF (20 ML) se añadió hidruro sódico al 95% (0,050 g, 2,0 mmol). Tras finalizar la adición, la mezcla se agitó a 0ºC durante 30 minutos y, después, a la mezcla de reacción se añadió 5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-carbaldehído (Ejemplo 212, preparado de un modo similar al procedimiento descrito más adelante, 0,340 g, 1,0 mmol). La mezcla resultante se agitó a temperatura ambiente durante 14 horas. Después de este tiempo, la mezcla de reacción se inactivó con una solución de cloruro amónico acuoso saturado (50 ml) y se extrajo con acetato de etilo. La capa orgánica se lavó con salmuera saturada, se secó sobre sulfato magnésico anhidro y se filtró. El filtrado se concentró y al residuo resultante se sometió a una cromatografía en columna en gel de sílice usando MeOH al 5% en cloroformo como eluyente, proporcionando 3-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il) acrilato de (E)-metilo (0,30 g, 72 %). CLEM Procedimiento V: tiempo de

retención 1,94 min [M+1] = 411,2.

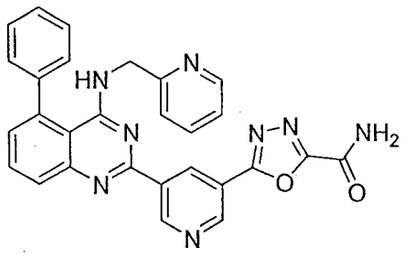
Etapa 2. Ejemplo 193



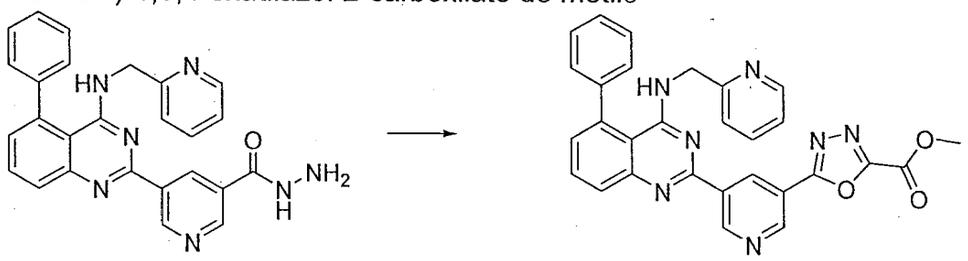
A una solución de 3-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il) acrilato de (E)-etilo (0,150 g, 0,370 mmol) en MeOH (25 ml) se añadió 10% de paladio sobre carbono (50 mg). La mezcla se agitó a temperatura ambiente en hidrógeno durante 14 horas. Después de este tiempo, la mezcla se filtró proporcionando el Ejemplo 193 (110 mg, 73%). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,21 (d, 1H, J = 4,4 Hz); 7,76-7,66 (m, 3H); 7,55-7,45 (m, 5H); 7,24-7,19 (m, 3H); 6,65 (a s, 1H); 4,54 (d, 2H, J = 4,4 Hz); 3,60 (s, 3H0; 3,06 (t, 2H, J = 6 Hz); 2,82 (t, 2H, J = 6 Hz). CLEM Procedimiento Y: tiempo de retención 1,87 min, [M+1] = 399,4; HPLC Procedimiento A1: pureza 94,0 %, tiempo de retención = 6,32 min.

EJEMPLO 194

5-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)-1,3,4-oxadiazol-2-carboxamida



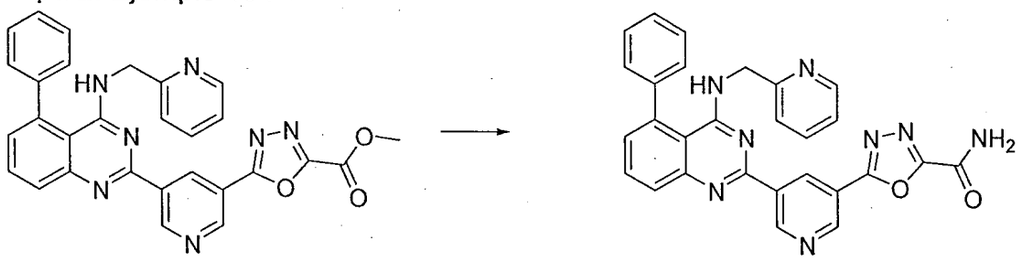
Etapa 1. Preparación de 5-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)-1,3,4-oxadiazol-2-carboxilato de metilo



A una solución de 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il) nicotinohidrazida (del Ejemplo 185, 0,30 g, 0,66 mmol) en DCM a 0ºC se añadió 2-cloro-2-oxoacetato de metilo (0,062 ml, 0,66 mmol) y carbonato potásico (0,273 g, 1,90 mmol). Tras finalizar la adición, la mezcla se agitó a temperatura ambiente durante 16 horas. Después de este tiempo, se añadió agua y la mezcla se extrajo en DCM, se secó y se concentró. El residuo resultante se disolvió en DCM. Se añadieron anhídrido tríflico (0,187 ml, 1,1 mmol) y piridina (0,149 ml, 1,8 mmol) y la mezcla resultante se agitó a temperatura ambiente durante 16 horas. Al finalizar este periodo, la mezcla de reacción se inactivó con agua y se extrajo con DCM (100 ml). La capa de DCM se lavó con agua y salmuera. La purificación cromatográfica proporcionó 5-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)-1,3,4-oxadiazol-2-carboxilato de metilo (270 mg, rendimiento del 78%) en

forma de un sólido blanco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,81 (s, 1H), 9,17 (s, 1H), 9,09 (s, 1H), 8,24 (d, *J* = 4,4 Hz, 1H), 7,94 (d, *J* =7,2 Hz, 1H), 7,86 (t, *J* = 7,6 Hz, 1H),7,75-7,72 (t, *J* = 7,6 Hz, 3H), 7,59-7,51 (m, 5H), 7,34 (d, *J* =7,2 Hz, 2H), 7,24 (t, *J* =6,4 Hz, 1H), 6,98 (t, *J* = 3,2 Hz, 1H), 4,77 (d, *J* = 4,0 Hz, 2H). CLEM Procedimiento Q: tiempo de retención 1,39 min; [M+1] = 514,5; HPLC Procedimiento B: pureza 98,1 %, tiempo de retención = 8,74 min.

Etapa 2. Ejemplo 194

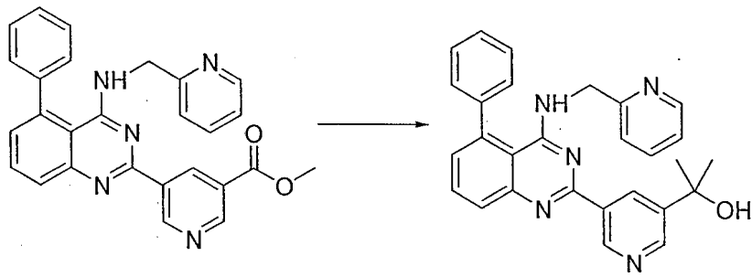


Una solución de 5-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)-1,3,4-oxadiazol-2-carboxilato de metilo (0,0700 g, 0,136 mmol) en NH_3 (2,0 M en MeOH, 10 ml) se calentó a 60ºC en un vaso sellado durante 4 horas. Después de este tiempo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente y el disolvente se evaporó a presión reducida, proporcionando el producto bruto. El producto bruto se recristalizó en EtOAc/hexanos proporcionando el Ejemplo 194 (0,06 g, rendimiento del 99%). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,81 (s, 1H), 9,17 (s, 1H), 9,09 (s, 1H), 8,24 (d, *J* = 4,4 Hz, 1H), 7,94 (d, *J* =7,2 Hz, 1H), 7,86 (t, *J* = 7,6 Hz, 1H),7,75-7,72 (t, *J* = 7,6 Hz, 3H), 7,59-7,51 (m, 5H), 7,34 (d, *J* =7,2 Hz, 2H), 7,24 (t, *J* =6,4 Hz, 1H), 6,98 (t, *J* = 3,2 Hz, 1H), 4,77 (d, *J* = 4,0 Hz, 2H). CLEM Procedimiento Q: tiempo de retención 1,39 min [M+1] = 499,50.

Procedimiento B HPLC: pureza 98,1 %, tiempo de retención = 8,74 min.

EJEMPLO 195

2-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)propan-2-ol

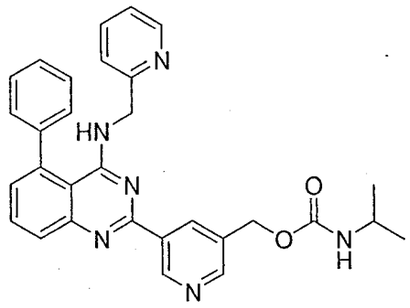


A una solución de 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)nicotinato de metilo (del Ejemplo 43, 0,30 g, 0,67 mmol) en THF (10 ml) se añadió yoduro de metilmagnesio (3,3 ml, 10 mmol) a 01C en atmósfera de nitrógeno. Tras finalizar la adición, la mezcla de reacción se agitó a temperatura ambiente durante 16 horas. Después de este tiempo, la mezcla de reacción se inactivó con la adición de agua y después se extrajo con acetato de etilo (50 ml). Los extractos orgánicos combinados se lavaron sucesivamente con agua y salmuera. La capa orgánica se secó, se filtró y se concentró. El residuo resultante se purificó mediante cromatografía en columna en gel de sílice (5% metanol en diclorometano), dando el Ejemplo 195 (0,090 g, rendimiento del 30 %) en forma de un sólido blanco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,51 (s, 1H), 8,81 (s, 1H), 8,79 (s, 1H), 8,25 (d, 1H, J = 4,4 Hz), 7,92 (d, 1H, J = 8,4Hz), 7,85 (dt, 1H, J= 7,2, 8Hz), 7,74 (m, 1H), 7,60-7,51(m, 5H), 7,34-7,31 (m, 2H), 7,29-7,22 (m, 1H), 7,24 (t, 1H, J =

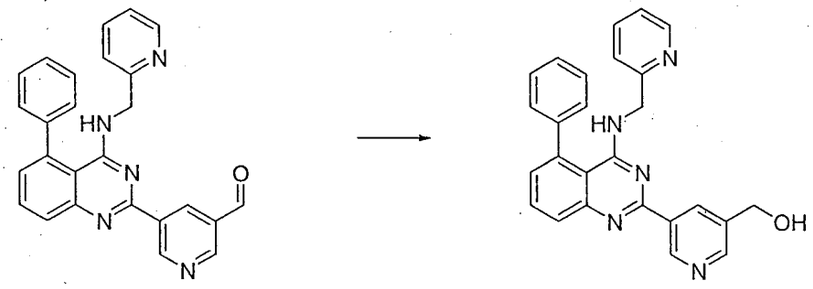
4,8, 7,6 Hz), 6,80 (s, 1H), 5,36 (s, 1H), 4,75 (d, 2H, *J*-4 Hz), 1,51 (s,6H). Procedimiento B HPLC: pureza 99,0%, tiempo de retención = 7,26 min; CLEM Procedimiento E: tiempo de retención 1,8 min [M+1] = 447,50.

EJEMPLO 196

Isopropilcarbamato de (5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)metilo



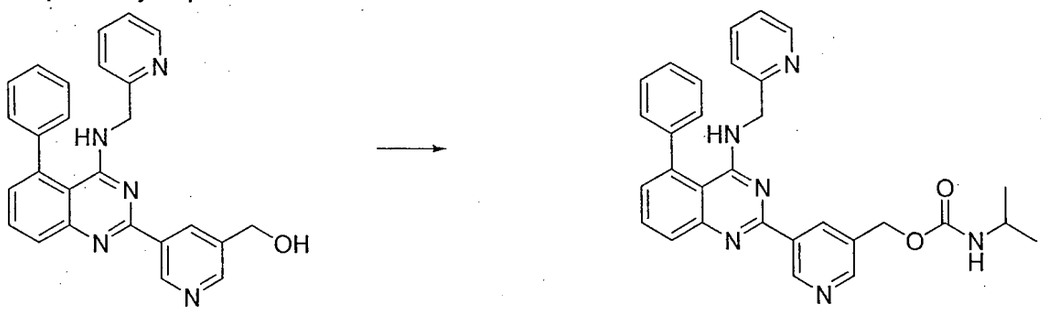
Etapa 1. Preparación de (5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)metanol



A una solución de 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il) nicotinaldehído (del Ejemplo 191, 1,0 g, 2,4 mmol) en etanol (15 ml) se añadió $NaBH_4$ (0,28 g, 7,19 mmol). Tras finalizar la adición, la mezcla de reacción se agitó a temperatura ambiente durante 4 horas. Después de este

tiempo se añadió una solución saturad de cloruro amónico y la mezcla resultante se extrajo en acetato de etilo. La capa orgánica se separó, se secó, se filtró y se concentró a presión reducida, dando un residuo. El residuo se purificó mediante cromatografía en columna en gel de sílice usando 2 % de metanol en DCM como eluyente, proporcionando (5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)metanol (0,71 g, rendimiento del 71 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,51 (s, 1H), 8,72 (s, 1H), 8,63 (s, 1H), 8,23 (d, 1H, J = 4,8 Hz), 7,88 (dd, 1H, J = 7,6 Hz, 8,4 Hz), 7,85 – 7,80 (m, 1H), 7,73 (dt, 1H, J = 1,2 Hz, 7,6 Hz), 7,61-7,48 (m, 5H), 7,33 (d, 2H, J =19,2 Hz), 7,27 (d, 1H, J =14 Hz), 7,23 (dt, 1H, J = 1,6, 7,2 Hz), 6,87 (t, 1H, J = 4,0 Hz, 1H), 5,47 (t, 1H, J= 5,6), 4,75 (d, 2H, J- 4 Hz), 4,67 (d, 2H, J = 5,6 Hz). CLEM Procedimiento U: tiempo de retención 1,46 min, [M+1] = 420,2; HPLC Procedimiento A2: pureza 99,5 %, tiempo de retención = 5,77 min.

Etapa 2. Ejemplo 196

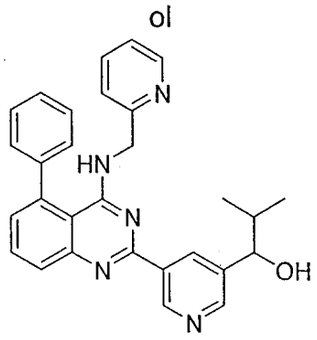


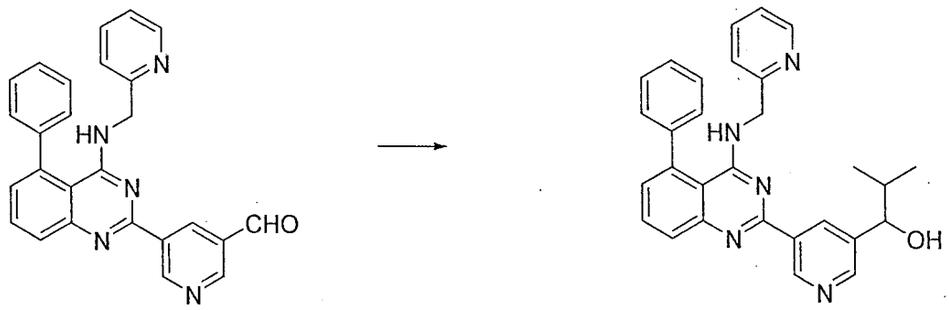
A una solución de 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)metanol (0,050 g, 0,12 mmol) en DCM (2 ml) se añadió DMAP (0,014 g, 0,12 mmol), seguido por isopropilisocianato (0,010 g, 0,12 mmol) a 0ºC. Tras finalizar la adición, la mezcla de reacción se calentó lentamente

hasta 45ºC, temperatura a la que se agitó durante 8 horas. Al finalizar este periodo, la mezcla de reacción se lavó con agua y se extrajo con acetato de etilo. Los extractos orgánicos combinados se secaron, se filtraron y se concentraron a presión reducida, dando un residuo. El residuo purificado mediante cromatografía en columna en gel de sílice (2% de MeOH en DCM), proporcionando el Ejemplo 196 (30 mg, rendimiento del 50%). RMN ^{1}H (400 MHz, DMSO-d_6) δ: 9,59 (s, 1H); 8,75 (s, 1H); 8,70 (s, 1H); 8,24 (d, 1H, J = 4,8 Hz); 7,88 9dd, 1H, J = 1,2, 8 Hz); 7,84 (t, 1H, J = 7,2 Hz); 7,73 (dt, 1H, J= 1,6, 7,6 Hz); 7,60-7,49 (m, 5H); 7,38-7,29 (m, 3H); 7,23 (dd, 1H, J = 1,6, 7,2 Hz); 6,87 (a s, 1H); 5,18 (a s, 1H); 4,75 (d, 2H, J = 4 HZ); 3,72-3,60 (m, 1H); 1,08 (d, 6H, J = 6,4 Hz). CLEM Procedimiento Y: tiempo de retención 2,00 min, [M+1] = 505,4; HPLC Procedimiento A1: pureza 98,9 %, tiempo de retención = 8,12 min.

EJEMPLO 197

2-metil-1-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)propan-1-ol





A una solución de 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il) nicotinaldehído (del ejemplo 191, 0,15 g, 0,35 mmol) en THF a -78° C se añadió cloruro de isopropilmagnesio (2 M en THF, 10 eq.). Tras finalizar la adición, la mezcla de reacción se dejó llegar a la temperatura ambiente. Una vez a la temperatura prescrita, la mezcla de reacción se agitó durante 16 horas. Después de este tiempo, la mezcla de reacción se inactivó con una solución saturada de cloruro amónico (2 ml) y después se extrajo con acetato de etilo. Las capas orgánicas combinadas se secaron, se concentraron a presión reducida y se purificaron mediante cromatografía en columna en gel de sílice (2% de MeOH en DCM) dando el Ejemplo 197 racémico (20 mg, rendimiento del 12 %). El racemato se separó en los correspondientes enantiómeros usando HPLC quiral, proporcionando el enantiómero 1 puro (4 mg) y el enantiómero 2 (3,5 mg), respectivamente. HPLC QUIRAL: (CHIRAL PAK IC (250 X 4.6) mm, 5micron; fase móvil (85% hexano, 15% etanol; caudal: 1ml/min}. ·Enantiómero 1: RMN ^{1}H (400 MHz, DMSO-d_6) δ: 9,51 (s, 1H); 8,69 (s, 1H); 8,60 (s, 1H); 8,26 (d, 1H, J = 4,4 Hz); 7,90 (d, 1H, J = 7,6 Hz); 8,55 (t, 1H, J = 7,2 Hz); 7,73 (dt, 1H, J = 1,6, 7,6 Hz); 7,61-7,50 (m, 4H); 7,38-7,30 (m, 2H); 7,24 (t, 1H, J = 9,2 Hz); 6,81 (a s, 1H); 5,42 (d, 1H, J =4,4 Hz); 4,74 (d, 2H, J = 4 Hz); 4,45 (t, 1H, J = 4,8 Hz); 2,00-2,90 (m, 1H); 0,92 (d,

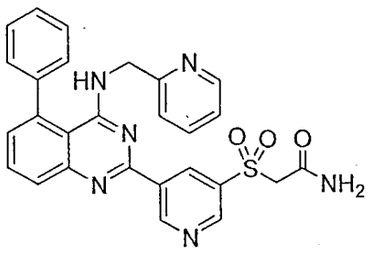
3H, *J* =6,4 Hz); 0,82 (t, 3H, *J* = 6,4 Hz). CLEM Procedimiento T: tiempo de retención 1,78 min, [M+1] = 462,2; HPLC Procedimiento A1: pureza 99,0%, tiempo de retención = 6,93 min.

HPLC QUIRAL: Tiempo de retención 19,78 ({CHIRAL PAK IC (250 X 4.6) mm, 5micron; fase móvil (hexano (85), etanol (15); caudal: 1ml/min}. Enantiómero 2:

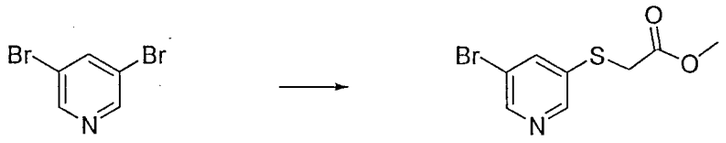
RMN ^{1}H (400 MHz, DMSO-d_6) δ: 9,51 (s, 1H); 8,69 (s, 1H); 8,60 (s, 1H); 8,26 (d, 1H, *J* = 4,4 Hz); 7,90 (d, 1H, *J* = 7,6 Hz); 8,55 (t, 1H, *J* = 7,2 Hz); 7,73 (dt, 1H, *J* = 1,6, 7,6 Hz); 7,61-7,50 (m, 4H); 7,38-7,30 (m, 2H); 7,24 (t, 1H, *J* = 9,2 Hz); 6,81 (a s, 1H); 5,42 (d, 1H, *J* =4,4 Hz); 4,74 (d, 2H, *J* = 4 Hz); 4,45 (t, 1H, *J* = 4,8 Hz); 2,00-2,90 (m, 1H); 0,92 (d, 3H, *J* =6,4 Hz); 0,82 (t, 3H, *J* = 6,4 Hz). CLEM Procedimiento T: tiempo de retención 1,78 min, [M+1] = 462,2; HPLC Procedimiento A1: pureza 96,9%, tiempo de retención = 6,93 min. CHIRAL HPLC: Tiempo de retención 22,02 ({CHIRAL PAK IC (250 X 4.6) mm, 5micron; fase móvil (hexano (85), etanol (15); caudal: 1ml/min}.

EJEMPLO 198

2-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)ilsufonil)acetamida

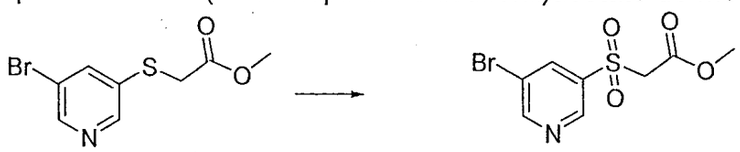


Etapa 1. Preparación de 2-(5-bromopiridin-3-iltio)acetato de metilo



A una solución de hidruro sódico (0,518 g, 21,0 mmol) en DMF (5 ml) a 0ºC se añadió, gota a gota, una solución de metiltioglicolato (2 g, 18 mmol) en DMF (6 ml). Tras finalizar la adición, la mezcla de reacción se agitó a temperatura ambiente durante 30 minutos. Después de este tiempo, gota a gota se añadió una solución de 3,5-dibromopiridina (4,46 g, 18 mmol) en DMF (10 ml). La mezcla de reacción resultante se dejó agitar a temperatura ambiente durante 16 horas. Al finalizar este periodo, la mezcla de reacción se inactivó mediante la adición de hielo y la suspensión espesa resultante se extrajo con acetato de etilo. Las capas orgánicas combinadas se secaron y se concentraron a presión reducida. El residuo resultante se purificó mediante cromatografía en columna en gel de sílice (1,5 % de metanol en DCM) dando 2-(5-bromopiridin-3-iltio) acetato de metilo (1,2 g, rendimiento del 24 %). LCME Procedimiento A: tiempo de retención 1,49 min [M+1] = 262.

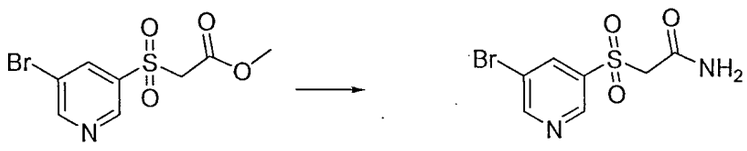
Etapa 2. Preparación de 2-(5-bromopiridin-3-ilsulfonil)acetato de metilo



A una solución de 2-(5-bromopiridin-3-iltio)acetato de metilo (1,2 g, 4,6 mmol) en MeOH:H_2O (12 ml) a una proporción de 3:1 se añadió oxona (2,8 g, 4,6 mmol). Tras finalizar la adición, la mezcla de reacción se agitó a

temperatura ambiente durante 5 horas. Al finalizar este periodo, la mezcla de reacción se concentró a presión reducida y después se extrajo con DCM. Las capas orgánicas combinadas se secaron y se concentraron a presión reducida, dando un residuo. El residuo se purificó mediante cromatografía en columna en gel de sílice (1,5 % de metanol en DCM) dando 2-(5-bromopiridin-3-ilsulfonil) acetato de metilo (0,6 g, rendimiento del 46 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ: 9,11 (d, 1H, J = 2Hz); 9,02 (d, 1H, J = 2 Hz); 8,57 (t, 1H, J = 2 Hz); 4,95 (s, 2H); 3,63 (s, 3H). CLEM Procedimiento T: tiempo de retención 1,12 min [M+1] = 294,0.

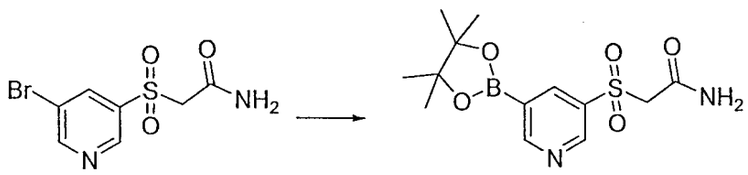
Etapa 3. Preparación de 2-(5-bromopiridin-3-ilsulfonil)acetamida



A una solución de 2-(5-bromopiridin-3-ilsulfonil)acetato de metilo (0,2 g, 0,67 mmol) se añadió 5% de amoniaco en metanol (10 ml). Tras finalizar la adición, la mezcla de reacción se agitó a 60ºC durante 4 horas. Después de este tiempo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente. Una vez a la temperatura prescrita, la mezcla de reacción se concentró a presión reducida, dando 2-(5-bromopiridin-3-ilsulfonil)acetamida (0,2 g) en forma de un sólido blanco. CLEM Procedimiento W: tiempo de retención 0,92 min [M-1] = 277,0

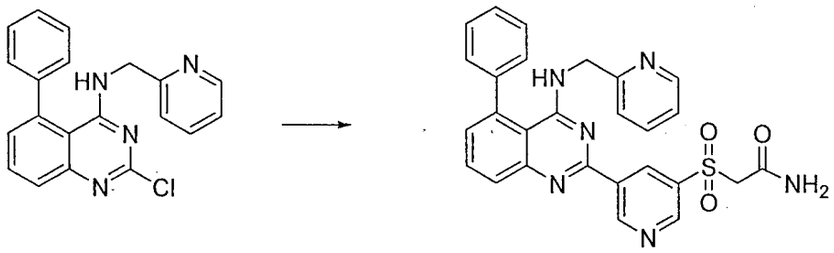
Etapa 4. Preparación de 2-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-piridin-

3-ilsulfonil)acetamida



Una mezcla de 2-(5-bromopiridin-3-ilsulfonil)acetamida (0,2 g, 0,7 mmol), bis(pinacolato)diboro (0,27 g, 1 mmol) y acetato potásico (0,2 g, 2,1 mmol) en 1,4-dioxano (10 ml) se desgasificó con nitrógeno durante 15 minutos. Después de este tiempo se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio(II) diclorometano (0,028 g, 0,35 mmol) y la mezcla resultante se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se calentó después en el microondas hasta 100ºC, durante 16 horas. Al finalizar este periodo, la mezcla de reacción se filtró a través de celite y el filtrado se concentró a presión reducida proporcionando 2-amino5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-ilsulfonil)acetamida (0,170 g), que se usó sin purificación adicional.

Etapa 5. Ejemplo 198

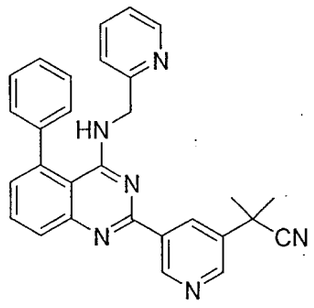


A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (del ejemplo 1, etapa 4, 0,182 g, 0.52 mmol) en 1,4-dioxano (6 ml) y H_2O (1,2

ml) en nitrógeno se añadió 2-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-ilsulfonil)acetamida (0,170 g, 0,57 mmol), y carbonato potásico (0,215 g, 1,56 mmol). Tras la finalización de la adición, la mezcla de reacción se desgasificó con nitrógeno durante 15 minutos. Después de este tiempo se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (0,042 g, 0,052 mmol). La mezcla resultante se desgasificó de nuevo con nitrógeno durante 10 minutos. Al finalizar este periodo, la mezcla de reacción se agitó a 100ºC durante 16 horas, después se dejó enfriar hasta la temperatura ambiente y se inactivó mediante la adición de agua. Tras finalizar la adición, la mezcla de reacción se transfirió a un embudo de separación y la capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El concentrado resultante se purificó mediante cromatografía en columna dando el Ejemplo 198 (0,020 g, rendimiento del 8 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ: 9,89 (s, 1H); 9,17 (s, 1H); 9,14 (s, 1H); 8,25 (s, 1H); 7,96 (dd, 1H, J = 1,6, 4,4Hz); 7,88 (dd, 1H, J = 7,2, 8,4Hz); 7,73 (dd, 1H, J = 2, 7,6 Hz); 7,61-7,50 (m, 5H); 7,45 (a s, 1H); 7,39-7,33 (m, 2H); 7,24 (t, 1H, J = 2,4 Hz); 6,96 (a s, 1H); 4,77 (d, 2H, J = 4Hz); 4,49 (s, 2H). CLEM Procedimiento Y: tiempo de retención 1,83 min, [M-1] = -509,0; HPLC Procedimiento A1: pureza 96,2 %, tiempo de retención = 6,79 min.

EJEMPLO 199

2-metil-2-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)propanonitrilo



Etapa 1. Preparación de 3-bromo-5-clorometilpiridina



A una solución de (5-bromo-piridin-3-il)-metanol (0,5 g, 2,68 mmol) en DCM (10 ml) se añadió cloruro de tionilo (0,5 ml). La solución resultante se agitó a temperatura ambiente durante 2 horas. Después de este tiempo, la mezcla de reacción se inactivó con agua y se extrajo en DCM. Los extractos orgánicos se lavaron con salmuera, se filtraron y se concentraron a presión reducida dando 3-bromo-5-clorometil-piridina (0,45 g, 82%), que se usó en la siguiente etapa sin purificación adicional.

Etapa 2. Preparación de 2-(5-bromopiridin-3-il)acetonitrilo

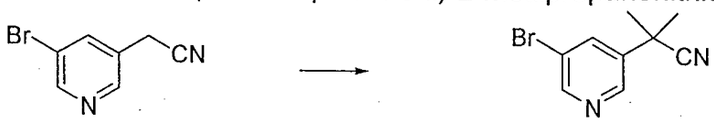


A una solución de 3-bromo-5-clorometil-piridina (0,45 g; 2,18 mmol) en

009925

DMF (10 ml) se añadió cianuro de potasio (0,21 g, 3,27 mmol). Tras finalizar la adición, la mezcla de reacción se agitó a temperatura ambiente durante 16 horas. Después de este tiempo, la mezcla de reacción se inactivó con agua y se extrajo con acetato de etilo. La fase orgánica se lavó con agua y salmuera, se secó sobre Na_2SO_4, se filtró y se evaporó. El residuo resultante se purificó mediante cromatografía en columna en gel de sílice (10 % de acetato de etilo en hexano) proporcionando 2-(5-bromopiridin-3-il) acetonitrilo (200 mg, 46,5 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,68 (d, 1H, J = 2 Hz), 8,51 (d, 1H, J = 2 Hz), 7,88 (t, 1H, J = 2 Hz), 3,77 (s, 2H).

Etapa 3. Preparación de 2-(5-bromopiridin-3-il)-2-metilpropanonitrilo

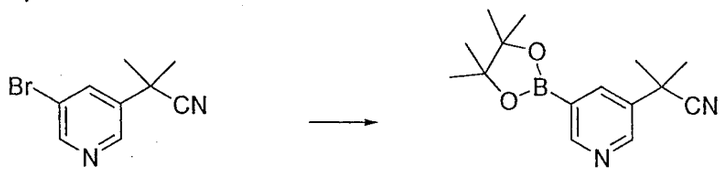


A una suspensión de NaH (95 %, 0,17 g, 7,1 mmol) en THF se añadió una solución de 2-(5-bromopiridin-3-il)acetonitrilo (0,7 g, 3,0 mmol) en THF (5 ml) a 0°C y la mezcla de reacción resultante se agitó a temperatura ambiente durante 30 minutos. Al finalizar este periodo, se añadió yoduro de metilo (0,66 ml, 8,9 mmol) y, después, la agitación continuó durante 16 horas adicionales. Después de este tiempo, la mezcla de reacción se inactivó mediante la adición de cloruro amónico saturado y después se extrajo en acetato de etilo. Las porciones orgánicas combinadas se concentraron a presión reducida y el residuo resultante se purificó mediante cromatografía en columna ultrarrápida (15% de acetato de etilo en hexanos) dando 2-(5-bromopiridin-3-il)-2-metilpropanonitrilo (0,35 g, 56 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm):

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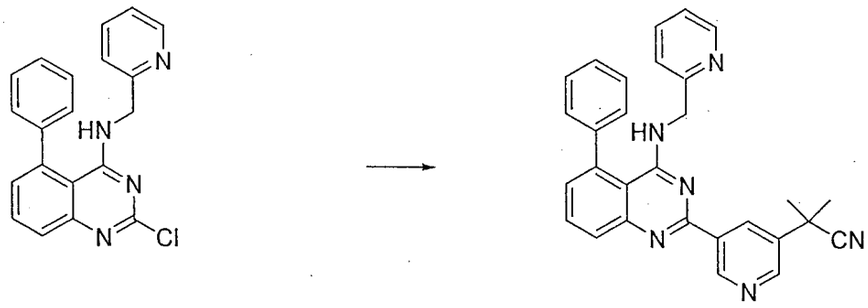
8,67 (d, 1H, *J* = 2 Hz),8,45 (d, 1H, *J* = 2 Hz), 7,73 (t, 1H, *J* = 2 Hz), 2,44 (s, 3H), 2,28 (s, 3H).

Etapa 4. Preparación de 2-metil-2-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-piridin-3-il)propanonitrilo



Una mezcla de 2-(5-bromopiridin-3-il)-2-metilpropanonitrilo (0,4 g, 1,77 mmol), bis(pinacolato)diboro (0,67 g, 2,65 mmol) y acetato potásico (0,69 g, 1,40 mmol) en 7,04-dioxano (10 ml) se desgasificó con nitrógeno durante 15 minutos. Después de este tiempo, se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio(II) diclorometano (0,11 g, 0,15 mmol). La mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno y después en el microondas hasta 120ºC, durante 45 minutos. Al finalizar este periodo, la mezcla de reacción se filtró a través de celite y el filtrado se concentró a presión reducida proporcionando 2-metil-2-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-il)propanonitrilo (0,53 g), que se usó sin purificación adicional.

Etapa 5. Ejemplo 199



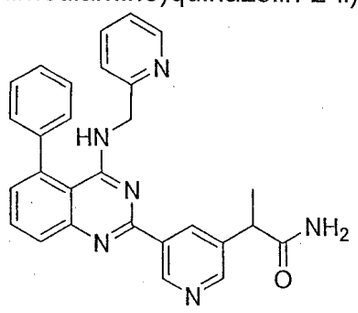
A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (del ejemplo 1, etapa 4, 0,4 g, 1 mmol) en 1,4-dioxano (15 ml) y H_2O (1 ml) en nitrógeno se añadió 2-metil-2-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-il)propanonitrilo (0,5 g, 2 mmol), y carbonato potásico (0,48 g, 3,5 mmol). Tras finalizar la adición, la mezcla se desgasificó con nitrógeno durante 15 minutos. Al finalizar este periodo se añadió el complejo cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (85 mg, 0,11 mmol) y la mezcla de reacción se desgasificó de nuevo con nitrógeno durante 10 minutos. Después de este tiempo, la mezcla de reacción se agitó a 95°C durante 16 horas. Al finalizar este periodo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente y después se inactivó mediante la adición de agua. Tras finalizar la adición, la mezcla de reacción se transfirió a un embudo de separación y la capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El residuo resultante se purificó mediante cromatografía en (2 % metanol en diclorometano), dando el Ejemplo 199 (0,38 g, rendimiento del 72 %) en forma de un sólido blancuzco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,61 (s, 1H), 8,92 (s, 1H), 8,88 (s, 1H), 8,24 (d, 1H, J = 4,4 Hz), 7,93 (dd, 1H, J =1,2 Hz, 4,4 Hz), 7,84 (t, 1H, J = 8 Hz),7,73 (dt, 1H, J = 1,6, 8 Hz), 7,63-7,50 (m, 5H),

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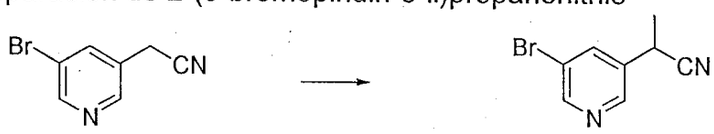
7,36-7,30 (m, 2H), 7,24 (t, 1H, *J* = 5,6 Hz), 6,84 (a s, 1H), 4,75 (d, 2H, *J* = 4,0 Hz), 1,84 (s, 6H). CLEM Procedimiento Y: tiempo de retención 2,04 min, [M+1] = 457,0; HPLC Procedimiento A1: pureza 99,1 %, tiempo de retención = 8,39 min.

EJEMPLO 200

2-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)propanamida



Etapa 1. Preparación de 2-(5-bromopiridin-3-il)propanonitrilo

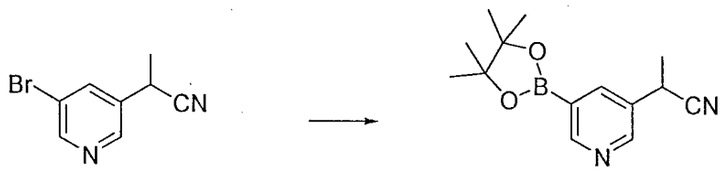


A una suspensión de NaH (95 %, 113 mg, 4,70 mmol) en DMF se añadió una solución de 2-(5-bromopiridin-3-il)acetonitrilo (del ejemplo 199, 0,8 g, 4 mmol) en DMF. Tras finalizar la adición, la mezcla de reacción se agitó a temperatura ambiente durante 30 minutos. Después de este tiempo, se añadió yoduro de metilo (0,3 ml, 4 mmol) y la agitación continuó durante 4 horas adicionales. Al finalizar este periodo, la mezcla de reacción se inactivó mediante la adición d una solución de cloruro amónico saturado y después se extrajo en acetato de etilo. Las porciones orgánicas combinadas se

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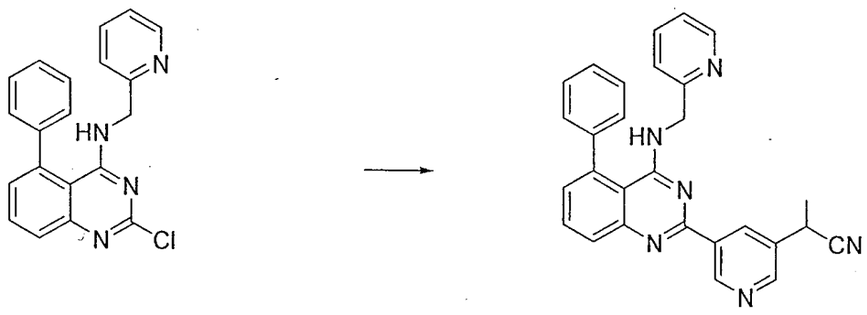
concentraron a presión reducida y el residuo resultante se purificó mediante cromatografía en columna ultrarrápida (30 % de EtOAc en hexanos) dando 2-(5-bromopiridin-3-il)propanonitrilo racémico (200 mg, 24 %). RMN ^{1}H (400 MHz, $CDCl_3$) δ (ppm): 8,67 (d, 1H, *J* = 2 Hz); 8,53 (d, 1H, *J* = 5 Hz); 7,88 (t, 1H, *J* = 5 Hz); 3,94 (c, 1H, *J* = 7,6 Hz); 1,69 (d, 3H, *J* = 7,6 Hz). CLEM Procedimiento Y: tiempo de retención 1,54 min [M+1] = 212,6.

Etapa 2. Preparación de 2-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-piridin-3-il)propanonitrilo



Una mezcla de 2-(5-bromopiridin-3-il)propanonitrilo (0,1 g, 0,5 mmol), bis(pinacolato)diboro (0,18 g, 0,70 mmol) y acetato potásico (0,19 g, 1,9 mmol) en 1,4-dioxano (8 ml) se desgasificó con nitrógeno durante 15 minutos. Después de este tiempo se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio(II) diclorometano (28 mg, 0,038 mmol) y la mezcla resultante se desgasificó de nuevo durante 10 minutos con nitrógeno. Al finalizar este periodo, la mezcla de reacción se calentó en el microondas a 120ºC durante 45 minutos. Después de este tiempo, la mezcla de reacción se filtró a través de celite y el filtrado se concentró a presión reducida proporcionando 2-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-il)propanonitrilo racémico (0,12 g), que se usó sin purificación adicional. CLEM Procedimiento Y: tiempo de retención 1,83 min [M+1] = 258,8.

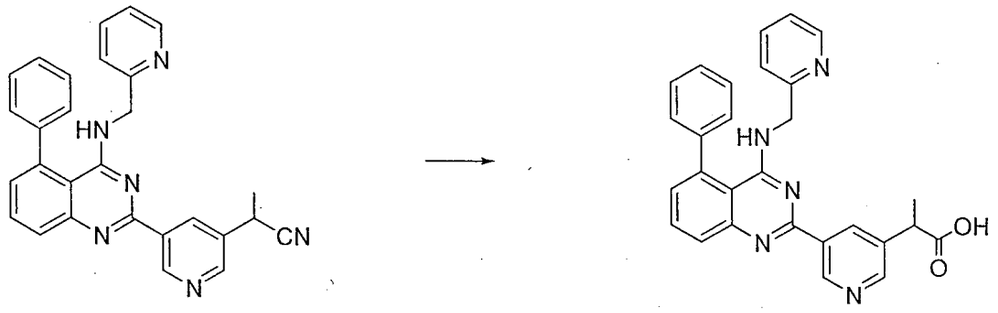
Etapa 3. Preparación de 2-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)propanonitrilo



A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (del ejemplo 1, etapa 4, 0,12 g, 0,5 mmol) en 1,4-dioxano (8 ml) y H_2O (0,55 ml) en nitrógeno se añadió 2-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-il)propanonitrilo (0,120 g, 0,4 mmol), y carbonato potásico (0,14 g, 1 mmol). La mezcla resultante se desgasificó con nitrógeno durante 15 minutos. Después de este tiempo, se añadió el complejo cloruro de 1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (0,26 mg, 0,036 mmol) y la mezcla de reacción se desgasificó de nuevo con nitrógeno durante 10 minutos. Al finalizar este periodo, la mezcla de reacción se agitó a 95°C durante 16 horas. Después, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente. Una vez a la temperatura prescrita, la mezcla de reacción se inactivó mediante la adición de agua y después se transfirió a un embudo de separación. La capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El concentrado resultante se purificó mediante cromatografía en columna en gel

de sílice usando 1 % de metanol en DCM, dando 2-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)propanonitrilo (95 mg, rendimiento del 63 %) en forma de un sólido blancuzco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,60 (s, 1H), 8,80 (d, 1H, J = 2 Hz); 8,77 (s, 1H); 8,26 (d, 1H, J = 6 Hz); 7,92 (dd, 1H, J = 1,2, 6,8 Hz); 7,85 (t, 1H, J = 6,8 Hz); 7,73 (dt, 1H, J = 1,6, 7,6 Hz); 7,58-7,52 (m, 5H); 7,34-7,32 (m, 2H); 7,24 (t, 1H, 7,2 Hz); 6,86 (t, 1H, J = 4 Hz); 4,76 (d, 2H, J = 4,4 Hz); 4,59 (c, 1H, J = 7,2 Hz); 1,68 (d, 3H, 7,2 Hz). CLEM Procedimiento Y: tiempo de retención 1,68 min [M+1] = 443,2.

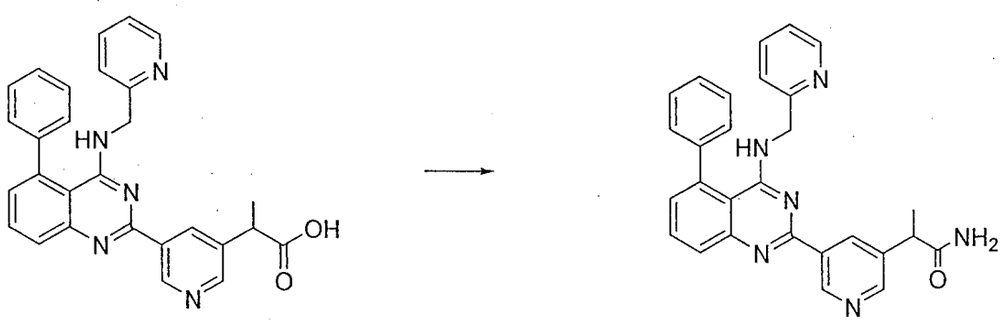
Etapa 4. Preparación de ácido 2-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)propanoico



A una solución de 2-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il) piridin-3-il)propanonitrilo racémico (0,08 g, 0,18 mmol) en etanol/agua (3,3 ml) se añadió NaOH sólido (52 mg, 1,1 mmol). Tras finalizar la adición, la mezcla de reacción se agitó a 95ºC durante 16 horas. Después de este tiempo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente y después se añadió agua (5 ml). Tras finalizar la adición se añadió HCl 1,0N a la mezcla de reacción para ajustar el pH A 6-7. Una vez al pH prescrito, la porción acuosa se extrajo con acetato de etilo. Los extractos orgánicos

combinados se secaron, se filtraron y se concentraron a presión reducida, dando ácido 2-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il) propanoico racémico (32 mg, rendimiento del 39 %).

Etapa 5. Ejemplo 200

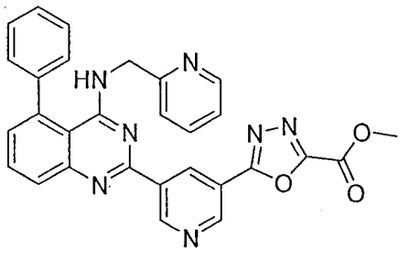


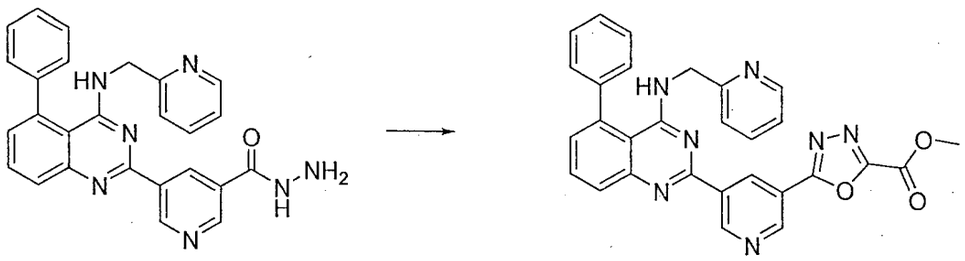
A una solución de ácido 2-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)propanoico racémico (0,08 g, 0.2 mmol) en DMF (1,5 ml) se añadió EDCI (0,04 g, 0,2 ml), HOBt (0,028 g, 0,20 mmol) y DIPEA (0,2 ml, 0,7 mmol), seguido por cloruro amónico (0,03 g, 0,7 mmol). La mezcla de reacción se agitó a temperatura ambiente durante 2 horas. Después de este tiempo, la mezcla de reacción se lavó y se extrajo con acetato de etilo. Los extractos orgánicos combinados se secaron, se filtraron y se concentraron a presión reducida. El residuo resultante se purificó mediante cromatografía en columna en gel de sílice ultrarrápida (5% metanol en diclorometano), obteniendo el Ejemplo 200 racémico (35 mg, rendimiento del 43 %) en forma de un sólido blancuzco. Los enantiómeros se separaron mediante Chiral HPLC (CHIRAL HPLC (CHIRAL PAK IC (250 X 4.6) mm, 5micron; fase móvil 85% hexano, 15% etanol; caudal: 1ml/min}). Enantiómero 1: RMN ^{1}H (400

MHz, DMSO-d_6) δ: 9,50 (s, 1H); 8,70 (s, 1H); 8,65 (s, 1H); 8,25 (d, *J*= 4,8 Hz, 1H), 7,91 (dd, *J*=1,2 Hz, 8,4 Hz, 1H), 7,84 (t, 7,2 Hz, 1H), 7,72 (dt, *J*= 1,6 Hz, 7,6 Hz, 1H), 7,62-7,50 (m, 6 Hz), 7,36-7,30 (m, 2H), 7,23 (dd, *J*= 5,2 Hz, 6,2 Hz, 1H), 6,98 (s, 1H), 6,83 (as, 1H), 4,74 (d, *J*= 4 Hz, 2H), 3,78 (t, *J*= 7,7 Hz, 1H), 1,44 (d, *J*= 7,2 Hz, 3H). CLEM Procedimiento Y: tiempo de retención 1,78 min, [M+1] = 461,0; HPLC Procedimiento A1: pureza 99,8 %, tiempo de retención = 6,04 min. CHIRAL HPLC: Tiempo de retención 15,43 {(CHIRAL PAK IC (250 X 4.6) mm, 5micron; fase móvil 85% hexano, 15% etanol; caudal: 1ml/min}. Enantiómero 2: RMN ^{1}H (400 MHz, DMSO-d_6) δ: 9,50 (s, 1H); 8,70 (s, 1H); 8,65 (s, 1H); 8,25 (d, *J*= 4,8 Hz, 1H), 7,91 (dd, *J*=1,2 Hz, 8,4 Hz, 1H), 7,84 (t, 7,2 Hz, 1H), 7,72 (dt, *J*= 1,6 Hz, 7,6 Hz, 1H), 7,62-7,50 (m, 6 Hz), 7,36-7,30 (m, 2H), 7,23 (dd, *J*= 5,2 Hz, 6,2 Hz, 1H), 6,98 (s, 1H), 6,83 (as, 1H), 4,74 (d, *J*= 4 Hz, 2H), 3,78 (t, *J*= 7,7 Hz, 1H), 1,44 (d, *J*= 7,2 Hz, 3H). CLEM Procedimiento Y: tiempo de retención 1,78 min, [M+1] = 461,0; HPLC Procedimiento A1: pureza 99,6 %, tiempo de retención = 6,06 min. CHIRAL HPLC: Tiempo de retención 19,08 {(CHIRAL PAK IC (250 X 4.6) mm, 5micron; fase móvil 85% hexano, 15% etanol; caudal: 1ml/min}.

EJEMPLO 201

5-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)-1,3,4-oxadiazol-2-carboxilato de metilo



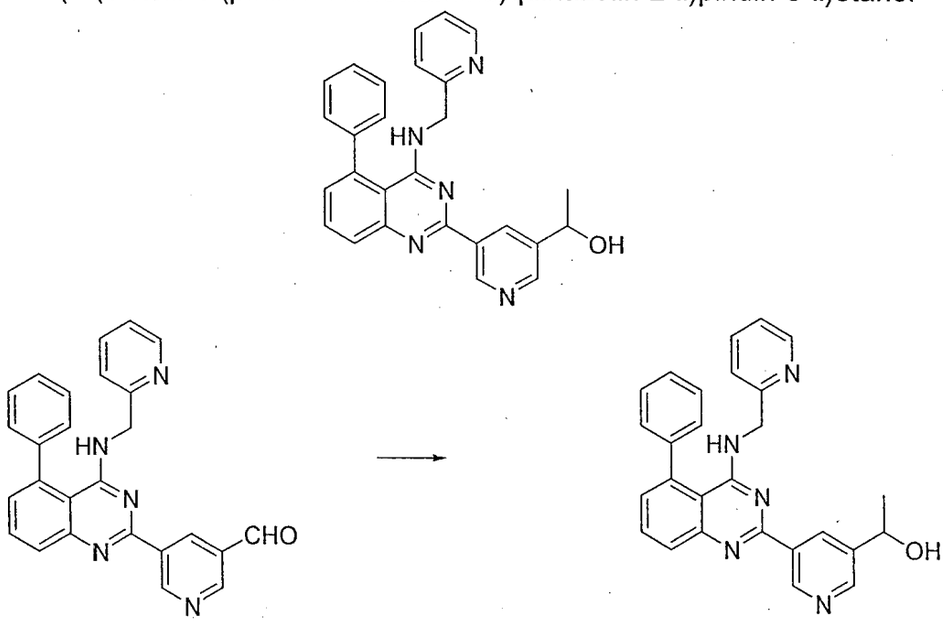


A una solución de 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il) nicotinohidrazida (del Ejemplo 185, 0,3 g, 0,66 mmol) en DCM (3 ml) a 0ºC se añadió 2-cloro-2-oxoacetato de metilo (0,062 ml, 0,66 mmol) y carbonato potásico (0,273 g, 1,90 mmol). Tras finalizar la adición, la mezcla de reacción se agitó a temperatura ambiente durante 16 horas. Después de este tiempo, se añadió agua (2 ml) y la mezcla de reacción se extrajo en DCM. Las porciones orgánicas combinadas se secaron y se concentraron a presión reducida. El residuo resultante se disolvió en DCM (3 ML) y se añadieron anhídrido trimetanosulfónico (0,19 ml, 1,1 mmol) y piridina (0,149 ml, 1,80 mmol). Tras finalizar la adición, la mezcla de reacción se agitó a temperatura ambiente durante 16 horas. Al finalizar este periodo, la mezcla de reacción se inactivó mediante la adición de agua y después se extrajo con DCM. Las porciones orgánicas combinadas se lavaron sucesivamente con agua y salmuera, se secaron, se filtraron y se concentraron a presión reducida dando un residuo. El residuo se purificó mediante cromatografía en columna ultrarrápida (2% de metanol en diclorometano), dando el Ejemplo 201 (270 mg, rendimiento del 35 %) en forma de un sólido blanco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,87 (s, 1H0; 9,36 (s, 1H0; 9,32 9s, 1H); 8,26 (d, 1H, J = 4,4 Hz), 7,98 (dd, 1H, J = 1,2, 8,4 Hz); 7,87 (dd, 1H, J = 1,4, 4 Hz); 7,74 (dt, 1H, J 1,6, 7,6 Hz); 7,62-7,50 (m, 5H); 7,39-7,31 (m, 2H); 7,24 (dd, 1H, J = 5,2, 6,8 Hz); 6,95 (a t, 1H, J = 4,4 Hz); 4,77 (d, 2H, J = 4 Hz); 4,05 (s, 3H). CLEM

Procedimiento Y: tiempo de retención 2,07 min, [M+1] = 516,0; HPLC Procedimiento A1: pureza 96,4 %, tiempo de retención = 8,75 min.

EJEMPLO 202

1-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)etanol

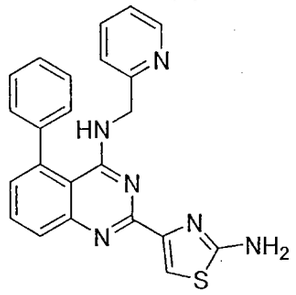


A una solución de 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il) nicotinaldehído (del ejemplo 191, 0,3 g, 0,7 mmol) en THF (5 ml) a 0º C se añadió una solución de bromuro de metilmagnesio (3 M en THF, 0,7 ml, 2 mmol). Tras finalizar la adición, la mezcla de reacción se agitó a temperatura ambiente durante 5 horas. Después de este tiempo, la mezcla de reacción se inactivó mediante la adición de solución saturada de cloruro amónico (2 ml) agua y después se extrajo en acetato de etilo. Las capas orgánicas combinadas se secaron, se filtraron y se concentraron dando un residuo. El residuo se purificó mediante cromatografía en columna dando el ejemplo 202

racémico (20 mg, rendimiento del 7%), que se separó en los enantiómeros correspondientes mediante HPLC quiral {CHIRAL PAK IC 250 X 4,6mm, 5micron; fase móvil 85% hexano , 15% etanol; Caudal: 1ml/min} para producir el enantiómero 1 puro (11 mg) y el enantiómero 2 (12 mg), respectivamente. Enantiómero 1: RMN ^{1}H (400 MHz, DMSO-d_6) δ: 9,50 (d, 1H, J = 2 Hz); 8,73 (s, 1H); 8,65 (d, 1H, J = 2 Hz); 8,24 (d, 1H, J = 4,8 Hz); 7,90 (dd, 1H, J = 1,2, 8,4 Hz); 7,83 (dd, 1H, J = 7,2, 8,4 Hz); 7,71 (dt, 1H, J = 1,6, 7,6 Hz); 7,60-7,49 (m, 5H); 7,38-7,27 (m, 2H); 7,23 (dd, 1H, J = 3,2, 6,8 Hz); 6,82 (a t, 1H, J = 4 Hz); 5,45 (d, 2H, J = 4 Hz); 4,92 (t, 1H, J = 3,6 Hz); 4,74 (d, 2H, J = 4 Hz); 1,45 (d, 3H, J = 6,8 Hz). CLEM Procedimiento V: tiempo de retención 1,60 min, [M+1] = 434,2; HPLC Procedimiento A1: pureza 99,8 %, tiempo de retención = 6,30 min. CHIRAL HPLC: Tiempo de retención 16,27 {(CHIRAL PAK IC (250 X 4.6) mm, 5micron; fase móvil 85% hexano, 15% etanol; caudal: 1ml/min}. Enantiómero 2: RMN ^{1}H (400 MHz, DMSO-d_6) δ: 9,50 (d, 1H, J = 2 Hz); 8,73 (s, 1H); 8,65 (d, 1H, J = 2 Hz); 8,24 (d, 1H, J = 4,8 Hz); 7,90 (dd, 1H, J = 1,2, 8,4 Hz); 7,83 (dd, 1H, J = 7,2, 8,4 Hz); 7,71 (dt, 1H, J = 1,6, 7,6 Hz); 7,60-7,49 (m, 5H); 7,38-7,27 (m, 2H); 7,23 (dd, 1H, J = 3,2, 6,8 Hz); 6,82 (a t, 1H, J = 4 Hz); 5,45 (d, 2H, J = 4 Hz); 4,92 (t, 1H, J = 3,6 Hz); 4,74 (d, 2H, J = 4 Hz); 1,45 (d, 3H, J = 6,8 Hz). CLEM Procedimiento T: tiempo de retención 1,61 min, [M+1] = 434,2; HPLC Procedimiento A1: pureza 96,8 %, tiempo de retención = 6,23 min. CHIRAL HPLC: Tiempo de retención 21,02 {(CHIRAL PAK IC (250 X 4.6) mm, 5micron; fase móvil 85% hexano, 15% etanol; caudal: 1ml/min}.

EJEMPLO 203

4-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)tiaxol-2-amina



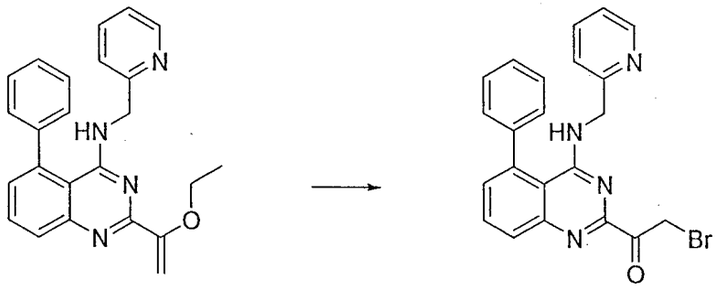
Etapa 1. Preparación de 2-(1-etoxivinil)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina



Al compuesto 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (1,0 g, 2,88 mmol) se añadió 1,4-dioxano (15 ml) y la solución resultante se desgasificó con nitrógeno. Se añadieron $Pd(TPP)_2Cl_2$ (0,202 g, 0,288 mmol) y tributil(1-etoxivinil)estannano (5,2 g, 14 mmol) en corriente de nitrógeno y la mezcla de reacción se calentó hasta 90ºC, temperatura a la cual se agitó durante 16 horas. Después de este tiempo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente. Una vez a la temperatura prescrita, la mezcla de reacción se concentró a presión reducida y el residuo resultante se purificó mediante cromatografía en columna de alúmina neutra (20% de acetato de etilo, hexano), parea dar 2-(1-etoxivinil)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (940 mg, rendimiento del 85 %) en forma de un sólido blanco. RMN ^1H (400 MHz, DMSO-d_6) δ (ppm): 8,23 (d, 1H, J = 4,4

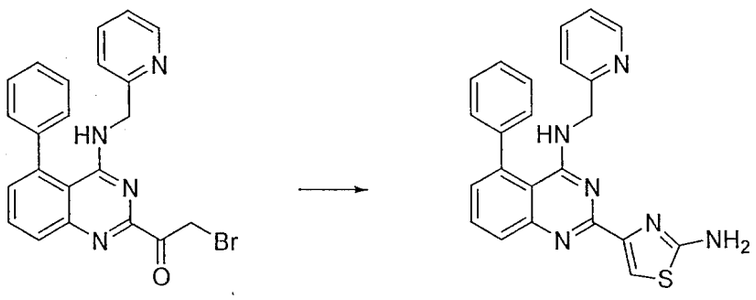
Hz), 7,75-7,85 (m, 2H), 7,70 (dt, 1H, *J* = 2, 7,6 Hz), 7,45-7,58 (m, 5H), 7,20-7,30 (m, 3H), 6,61 (a s, 1H), 4,61 (s, 1H), 4,60 (d, 2H, *J* = 4Hz), 3,94 (c, 2H, *J* = 6,8 Hz), 1,40 (t, 3H, *J* = 6,8 Hz). CLEM Procedimiento Y: tiempo de retención 1,952 min [M+1] = 383,2.

Etapa 2. Preparación de 2-bromo-1-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)etanona



A 1,4-dioxano/agua (3:1) (20 ml) se añadió N-bromosuccinimida (0,55 g, 3,1 mmol). Después se añadió 2-(1-etoxivinil)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,59 g, 1,5 mmol) en porciones pequeñas a 0ºC. Tras finalizar la adición, la mezcla de reacción se agitó a temperatura ambiente durante 20 horas. Después de este tiempo, se añadió agua y la porción acuosa se extrajo dos veces con DCM. Las capas orgánicas combinadas se secaron, se filtraron y se evaporaron a presión reducida dando 2-bromo-1-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)etanona (600 mg, pureza del 69 % mediante CLEM), que se usó sin purificación adicional. CLEM Procedimiento Y: tiempo de retención 1,996 min [M+1] = 433.

Etapa 3. Ejemplo 203

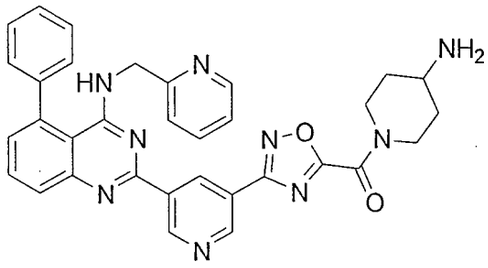


A una solución de 2-bromo-1-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)etanona (75 mg, 0,17 mmol) en etanol (7 ml) se añadió tiourea (14 mg, 0,17 mmol) y la mezcla de reacción se calentó hasta 70ºC durante 1 hora. Después de este tiempo, el etanol se evaporó a presión reducida y se añadió DCM (25 ml). Tras finalizar la adición, la porción orgánica se lavó con solución de bicarbonato sódico al 10% y la capa acuosa se extrajo con DCM (2 x 20 ml). Las fases orgánicas combinadas se secaron y se evaporaron a presión reducida, dando un residuo. El residuo se purificó mediante cromatografía en gel de sílice (8% de metanol en diclorometano), proporcionando el Ejemplo 203 (25 mg, 35%) en forma de un semisólido negro. RMN ^{1}H (400 MHz, DMSO-d_6) δ: 8,24 (d, 1H, J = 4,8 Hz); 7,80-7,67 (m, 3H); 7,45-7,59 (m, 6H); 7,20-7,30 (m, 3H); 7,07 (s, 2H); 6,56 (a s, 1H); 4,65 (d, 2H, J = 4,4 Hz). CLEM Procedimiento V: tiempo de retención 1,59 min, [M+1] = 411,2; HPLC Procedimiento A1: pureza 97,6 %, tiempo de retención = 6,52 min.

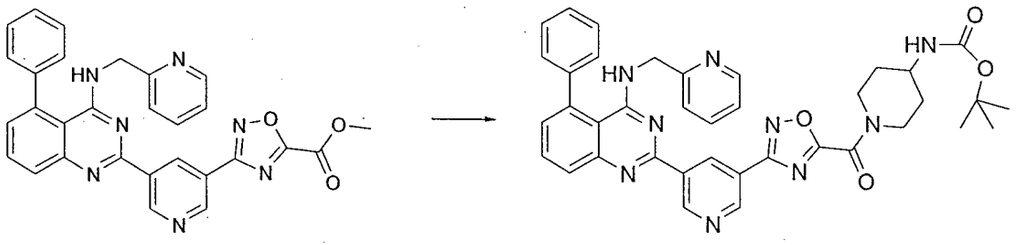
EJEMPLO 204

(4-aminopiperidin-1-il)(3-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)-1,2,4-oxadiazol-5-il)metanona

P00940

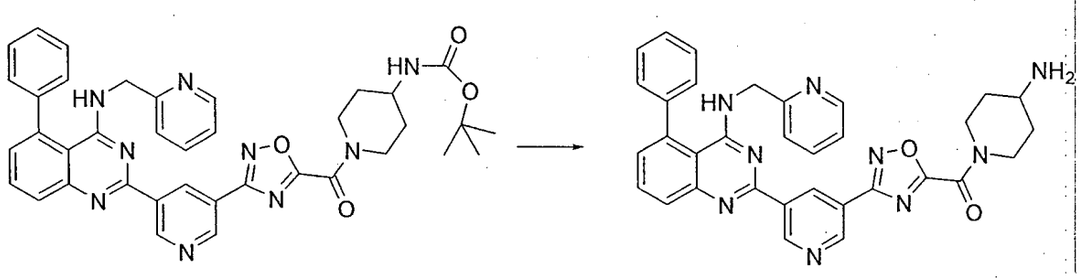


Etapa 1. Preparación de 1-(3-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)-1,2,4-oxadiazol-5-carbonil)piperidin-4-ilcarbamato de terc-butilo



A una solución de 3-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)-1,2,4-oxadiazol-5-carboxilato de metilo (del ejemplo 187, 0,2 g, 0,38 mmol) en etanol (10 ml) se añadió 4-(Boc-amino)piperidina (0,389 g, 1,90 mmol). Tras finalizar la adición, la mezcla de reacción se calentó hasta 80ºC, temperatura a la que se agitó durante 16 horas. Al finalizar este periodo, el etanol se evaporó y el residuo resultante se purificó mediante cromatografía en columna ultrarrápida en gel de sílice (1,6% metanol en DCM) dando 1-(3-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)-1,2,4-oxadiazol-5-carbonil)piperidin-4-ilcarbamato de terc-butilo (0,1 g, rendimiento del 38%) en forma de un sólido amarillo. CLEM Procedimiento T: tiempo de retención 2,08 min [M+1] = 684,2.

Etapa 2. Ejemplo 204

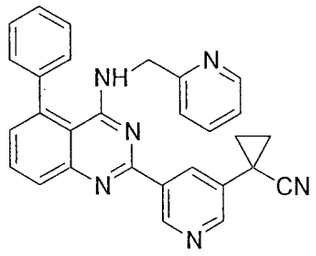


A una solución de 1-(3-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)-1,2,4-oxadiazol-5-carbonil)piperidin-4-ilcarbamato de terc-butilo (0,1 g, 0,1 mmol) en éter (3 ml) se añadió éter HCl (2 ml). La mezcla de reacción se agitó a temperatura ambiente durante 16 horas. Después de este tiempo se formó un precipitado y la solución se decantó en la mezcla de reacción. El sólido resultante se recristalizó en éter dando el ejemplo 204 (0,022 g, rendimiento del 26%). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 954 (s, 1H), 826 (d, 1H, J = 4 Hz); 796 (dd, 1H, J = 12, 8 Hz); 787 (dd, 1H, J = 72, 8 Hz); 772 (dd, 1H, J = 16, 76 Hz); 763 -750 (m, 2H); 739-733 (m, 2H); 725 (t, 1H, J = 56 Hz); 695 (a s, 1H); 477 (d, 2H, J = 2 Hz); 430 (a d, 1H, J = 12 Hz); 402 (a d, 1H, J = 12 Hz); 340-336 (m, 1H); 321-313 (m, 1H); 304-295 (m, 1H); 195-180 (m, 2H); 143-128 (m, 2H). CLEM Procedimiento T: tiempo de retención 1,65 min, [M+1] = 584,2; HPLC Procedimiento A1: pureza 96,1%, tiempo de retención = 6,08 min.

EJEMPLO 205

1-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-

il)ciclopropanocarbonitrilo



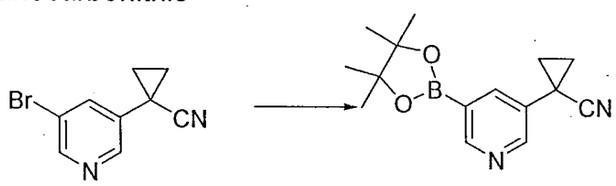
Etapa 1. Preparación de 1-(5-bromopiridin-3-il)-ciclopropanonitrilo



Una suspensión de 7 ml de NaOH (50/50 p/p en H_2O) se cargó con 2-(5-bromopiridin-3-il)acetonitrilo (del ejemplo 199: 0,36 g, 1,9 mmol). Se añadió 1-bromo-2-cloroetano (0,29 g, 2,10 mmol), seguido por una cantidad catalítica de cloruro de benciltrietilamonio (5 mg). La mezcla de reacción se agitó durante 20 horas a 60ºC y después se vertió en agua. La solución resultante se extrajo en acetato de etilo. Los extractos combinados se lavaron sucesivamente con agua y salmuera, se secaron sobre Na_2SO_4, se filtraron y después se concentraron dando 1-(5-bromopiridin-3-il)ciclopropanocarbonitrilo (0,25 g, 41 %), que se usó sin purificación adicional. RMN ^1H (400 MHz, $CDCl_3$) δ (ppm): 8,49 (d, 1H, *J* = 2 Hz); 7,78 (d, 1H, *J* = 4 Hz); 3,94 (c, 2H, *J* = 7,6 Hz); 1,69 (d, 3H, *J* = 7,6 Hz). CLEM Procedimiento Y: tiempo de retención 1,54 min [M+1] = 212,6.

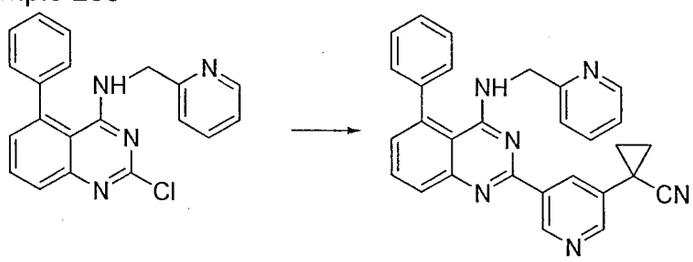
Etapa 2. Preparación de 1-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-piridin-

3-il)ciclopropanocarbonitrilo



Una mezcla de 1-(5-bromopiridin-3-il)ciclopropanonitrilo (0,25 g, 1,1 mmol), bis(pinacolato)diboro (0,31 g, 1,2 mmol) y acetato potásico (0,44 g, 4,5 mmol) en 1,4-dioxano (8 ml) se desgasificó con nitrógeno durante 15 minutos. Después de este tiempo se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio(II) diclorometano (94 mg, 0,12 mmol) y la mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se calentó después en el reactor microondas a 120ºC, durante 45 minutos. Al finalizar este periodo, la mezcla de reacción se filtró a través de celite y el filtrado se concentró a presión reducida proporcionando 1-amino5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-il)ciclopropanonitrilo (0,28 g), que se usó sin purificación adicional. CLEM Procedimiento Y: tiempo de retención 1,83 min [M+1] = 258,8.

Etapa 3. Ejemplo 205

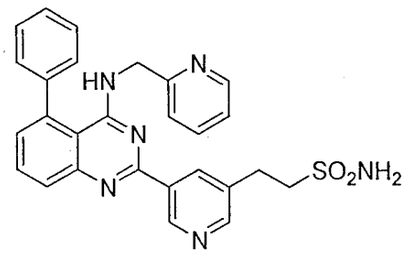


A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (del ejemplo 1, etapa 4, 0,12 g, 0,34 mmol) en 1,4-dioxano (8 ml) y H_2O (0,55

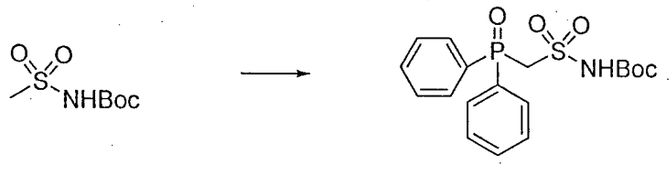
ml) en nitrógeno se añadió 1-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-il)ciclopropanonitrilo (0,12 g, 0,37 mmol), y carbonato potásico (0,15 g, 1,11 mmol). La mezcla de reacción se desgasificó con nitrógeno durante 15 minutos. Se añadió el complejo cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (27 mg, 0,037 mmol) y la mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se agitó a 95ºC durante 16 horas, después se dejó enfriar hasta la temperatura ambiente y se inactivó mediante la adición de agua. La mezcla de reacción se transfirió a un embudo de separación y la capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El residuo resultante se purificó mediante cromatografía en (2 % metanol en DCM), dando el Ejemplo 205 (85 mg, rendimiento del 55 %) en forma de un sólido blancuzco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,57 (s, 1H), 8,80 (d, 1H, J = 2Hz); 8,77 (s, 1H); 8,26 (d, 1H, J = 6 Hz); 7,92 (dd, 1H, J = 1,2, 6,8 Hz); 7,85 (t, 1H, J = 6,8 Hz); 7,73 (dt, 1H, J = 1,6, 7,6 Hz); 7,58-7,52 (m, 5H); 7,34-7,32 (m, 2H); 7,24 (t, 1H, 7,2 Hz); 6,86 (t, 1H, J = 4 Hz); 4,75 (d, 2H, J = 4,4 Hz); 1,90 (dd, 2H, J = 4,8, 8 Hz); 1,90 (dd, 2H, J = 4,8, 8 Hz). CLEM Procedimiento V: tiempo de retención 1,78 min, [M+1] = 455,2; HPLC Procedimiento A1: pureza 97,7 %, tiempo de retención = 7,75 min.

EJEMPLO 206

2-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)etanosulfonamida

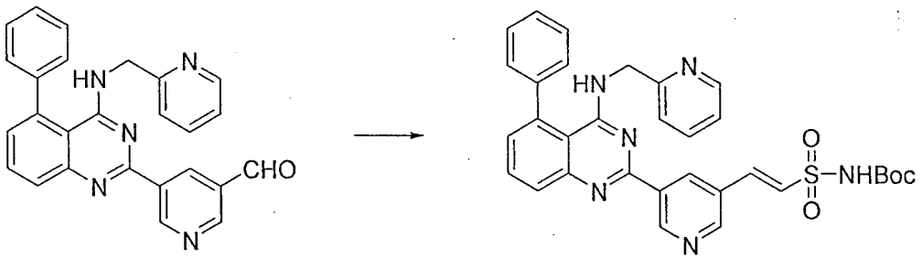


Etapa 1. Preparación de terc-butil(difenilfosforil)metilsulfonilcarbamato



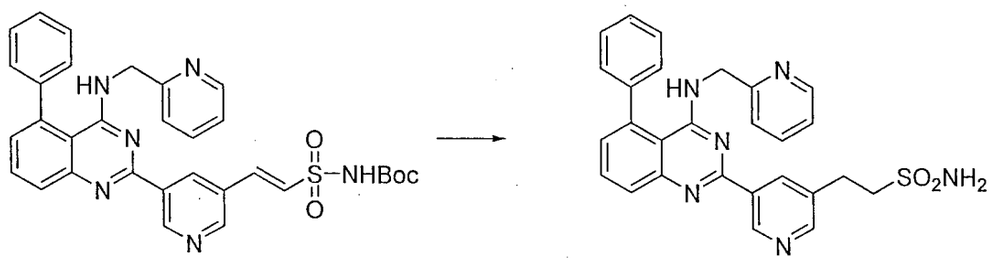
A una solución de metilsulfonilcarbamato de terc-butilo (2 g, 10 mmol) en THF (25 ml) a -78ºC se añadió LDA (2M en THF, 15,4 ml, 30,7 mmol). Tras finalizar la adición, la mezcla de reacción se agitó durante 10 minutos y después, gota a gota, se añadió cloruro difenilfosfínico (2,42 g, 10,2 mmol) a la reacción a -78ºC. Después de 90 minutos, se añadió agua (100 ml) y la mezcla de reacción se diluyó con acetato de etilo (250 ml). La capa acuosa se ajustó hasta pH 5 con 5% de HCl acuoso. El precipitado blanco que se formó se filtró y el sólido se secó al vacío dando terc-butil(difenilfosforil)metilsulfonilcarbamato (2,9 g, rendimiento del 72%) en forma de un sólido blanco.

Etapa 2. Preparación de 2-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)vinilsulfonilcarbamato de (E)-terc-butilo



Una solución de {[(difenilfosforil)metil]sulfonil}carbamato de terc-butilo (0,400 g, 1,01 mmol) en N,N-dimetilformamida (20 ml) se añadió hidruro sódico al 95% (0,06 g, 2 mmol) y la mezcla de reacción se agitó a 0ºC durante 1 hora. A la mezcla de reacción se añadió 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)nicotinaldehído (del ejemplo 191: 0,505 g, 1,21 mmol) y la mezcla resultante se agitó a temperatura ambiente durante 18 horas. A la mezcla de reacción se añadió una solución de cloruro amónico acuoso saturado (100 ml) y la mezcla resultante se extrajo con acetato de etilo. Las capas orgánicas combinadas se lavaron con salmuera saturada, se secaron sobre sulfato magnésico anhidro y se filtraron. El filtrado se concentró y el residuo resultante se sometió a cromatografía en columna en gel de sílice ($CHCl_3$-MeOH 95:5). El material resultante se cristalizó de CH_2Cl_2-hexano dando el 2-(5-(5-fenil-4-(piridin-2-ilmetilamino) quinazolin-2-il) piridin-3-il) vinilsulfonilcarbamato de (E)-terc-butilo (0,450 g, rendimiento del 62 %) en forma de un sólido marrón. CLEM Procedimiento Y: tiempo de retención 1,90 min [M+1] = 595,4.

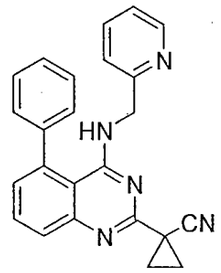
Etapa 3. Ejemplo 206



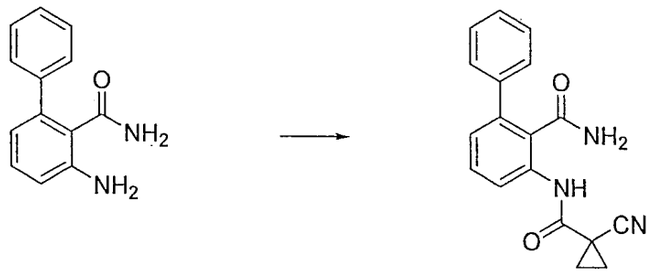
A una solución de 2-(5-fenil-4-(piridin-2-ilmetilamino) quinazolin-2-il)vinilsulfonilcarbamato de (E)-terc-butilo (0,210 g, 0,410 mmol) en MeOH (10 ml) se añadió 10% de paladio sobre carbono (20 mg) y la mezcla de reacción se agitó a temperatura ambiente en una atmósfera de hidrógeno durante 14 horas. La mezcla de reacción se filtró y el filtrado se concentró a presión reducida, dando un residuo. Al residuo se añadió ácido trifluoroacético (15 ml) y la mezcla de reacción se agitó a temperatura ambiente durante 2 horas. Después de este tiempo, la mezcla de reacción se concentró a presión reducida, se añadió bicarbonato sódico y la mezcla resultante se extrajo con acetato de etilo. Las capas orgánicas combinadas se lavaron con salmuera saturada, se secaron sobre sulfato magnésico anhidro y se filtraron. El filtrado se concentró y el residuo resultante se sometió a cromatografía en columna en gel de sílice ($CHCl_3$-MeOH 95:5), seguido por recristalización ($CHCl_3$-hexano) dando el ejemplo 206 (0,115 g, 65%) en forma de un sólido blanco. RMN ^1H (400 MHz, DMSO-d_6) δ (ppm): 9,49 (as, 1H), 8,63 (am, 2H), 8,27 (m, 1H), 7,91-7,82 (m, 2H), 7,74 (m, 1H), 7,59-7,55 (m, 5H),7,28-7,21 (m,1H), 6,95 (m, 2H), 6,82 (as, 1H), 4,75 (d, J = 4,0 Hz, 2H), 3,42 (t, J= 5,6 Hz, 2H), 3,21 (t, J= 8 Hz, 2H). CLEM Procedimiento Y: tiempo de retención 1,59 min, [M+1] = 497,2; HPLC Procedimiento A1: pureza 99,6 %, tiempo de retención = 7,96 min.

EJEMPLO 207

1-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)ciclopropanocarbonitrilo



Etapa 1.preparación de 3-(1-cianociclopropanocarboxamido)bifenil-2-carboxamida

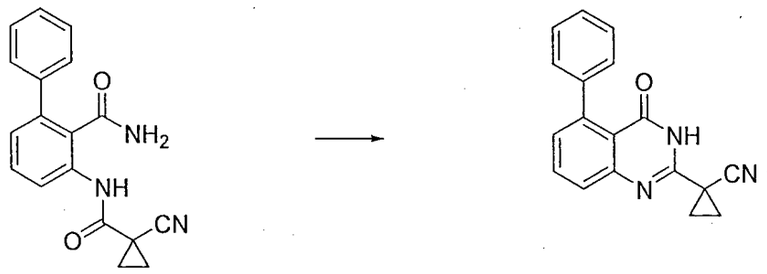


A una solución de ácido 1-cianociclopropanocarboxílico (0,75 g, 7 mmol) en DCM (40 ml) se añadió HTU (3,5 mg, 10 mmol) y DIPEA (3,4 ml, 20 mmol). Después de agitar a temperatura ambiente durante 1 hora, se añadió 3-aminobifenil-2-carboxamida (del ejemplo 218: 1 g, 5 mmol) y la mezcla de reacción se agitó durante 16 horas adicionales. La mezcla de reacción se lavó con agua y la fase orgánica se secó, se filtró, se concentró a presión reducida y se purificó mediante cromatografía en gel de sílice (60% de acetato de etilo

000949

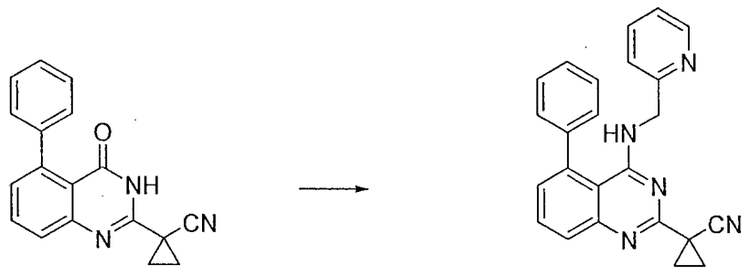
en hexanos) proporcionando 3-(1-cianociclopropanocarboxamido)bifenil-2-carboxamida (0,75 g, rendimiento del 74%) en forma de un sólido blanco. CLEM Procedimiento T: tiempo de retención 1,53 min [M+1] = 306,2.

Etapa 2. Preparación de 1-(4-oxo-5-fenil-3,4-dihidroquinazolin-2-il)ciclopropanocarbonitrilo



A una solución de 3-(1-cianociclopropanocarboxamido)bifenil-2-carboxamida (0,7 g, 2 mmol) en metanol se añadió Na_2CO_3 (23 mmol) acuoso saturado y la mezcla de reacción se agitó a 80°C durante 30 minutos. La mezcla de reacción se concentró a presión reducida y el residuo resultante se diluyó con acetato de etilo, después se lavó con agua. Los extractos orgánicos se secaron, se concentraron y se purificaron mediante cromatografía en gel de sílice (4% de MeOH en DCM) dando 1-(4-oxo-5-fenil-3,4-dihidroquinazolin-2-il)ciclopropanocarbonitrilo (0,65 g, rendimiento del 99 %) en forma de un sólido blanco. CLEM Procedimiento T: tiempo de retención 1,810 min [M+1] = 288,2.

Etapa 3. Ejemplo 207

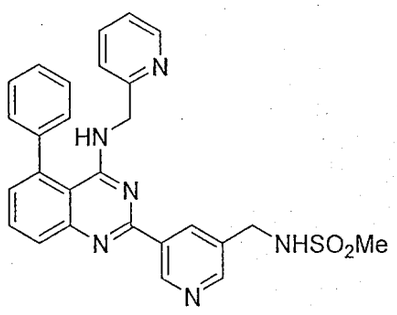


A una solución de 1-(4-oxo-5-fenil-3,4-dihidroquinazolin-2-il)ciclopropanocarbonitrilo) (0,15 g, 0,52 mmol) en acetonitrilo (3 ml) a temperatura ambiente se añadió DBU (0,25 g, 1,6 mmol) y BOP (0,3 g, 0,7 mmol) y la mezcla de reacción se agitó durante 30 minutos. Se añadió aminometilpiridina (0,1 ml, 0,93 mmol) y la mezcla de reacción resultante se agitó durante 16 horas adicionales. La mezcla de reacción se concentró a presión reducida y el residuo resultante se purificó mediante cromatográfica en columna en gel de sílice (2% de MeOH en DCM) dando el Ejemplo 207 (0,05 g, rendimiento del 25%) en forma de sólido blanco. RMN ^{1}H (400 MHz, DMSO-d_6) δ: 8,23 (s, 1H); 7,82-7,62 (m, 3H); 7,60-7,46 (m, 5H); 7,21-7,28 (m, 3H); 6,76 (t, 1H, J = 4 Hz); 4,52 (d, 2H, J = 4 Hz); 1,78-1,74 (m, 4H). CLEM CL-EM Procedimiento V: tiempo de retención 1,80 min, [M+1] = 378,2; HPLC Procedimiento A1: pureza 95,2 %, tiempo de retención = 8,75 min.

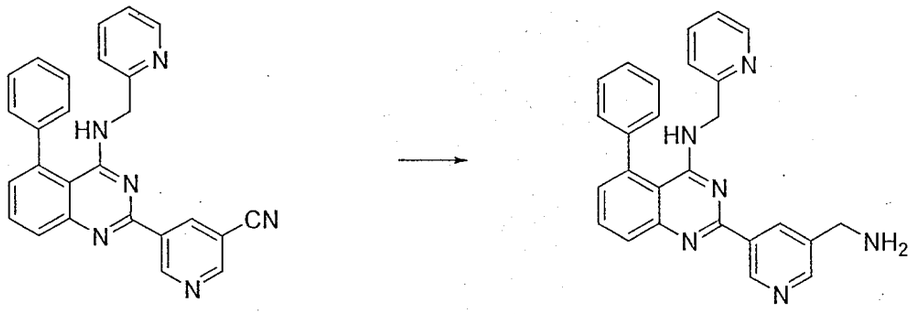
EJEMPLO 208

N-((5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)metil)metanosulfonamida

009951

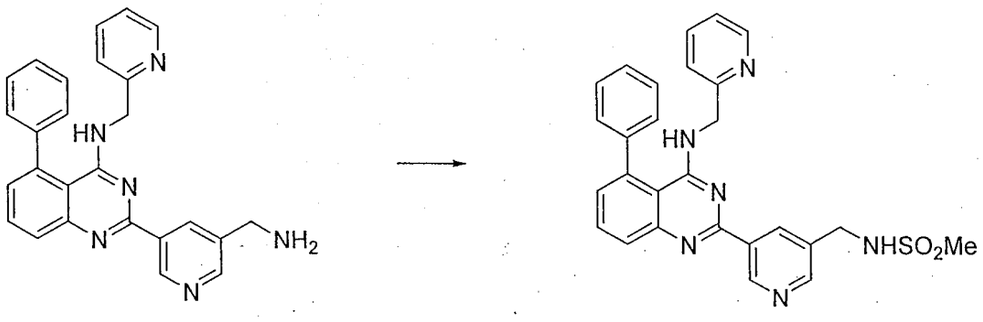


Etapa 1. Preparación de 2-(5-aminometil)piridin-3-il)-5-fenil-N(piridin-2-ilmetil)-quinazolin-4-amina



A una solución de 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)nicotinonitrilo (del ejemplo 183: 200 mg, 0,48 mmol) en 5 % de amoniaco en metanol (5 ml) se añadió Ra-Ni (catalítico) y la suspensión espesa resultante se agitó en atmósfera de hidrógeno durante 16 horas. Después de este tiempo, la mezcla de reacción se filtró y el filtrado se concentró a presión reducida dando 2-(5-(aminometil)piridin-3-il)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,1 g, rendimiento del 50 %), que se usó sin purificación adicional.

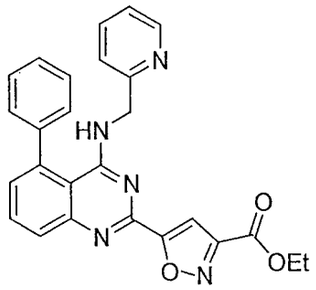
Etapa 2. Ejemplo 208

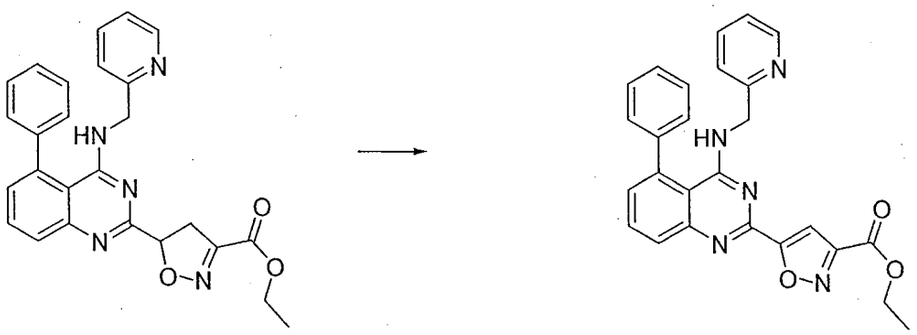


A una solución agitada de 2-(5-(aminometil)piridin-3-il)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,1 g, 0,2 mmol) y TEA (0,063 ml, 0,46 mmol) en DCM (3 ml) se añadió cloruro de metanosulfonilo (0,24 ml, 0,3 mmol) gota a gota a 0ºC. La mezcla de reacción se agitó durante 1 hora y después se inactivó mediante la adición de agua (1 ml). La solución resultante se extrajo con DCM. Los extractos orgánicos combinados se lavaron sucesivamente con agua y salmuera, y se secaron sobre Na_2SO_4, se filtraron y el filtrado se concentró a presión reducida. El residuo resultante se sometió a cromatografía en gel de sílice (MeOH/DCM, 2:98) proporcionando el Ejemplo 208 (40 mg, 34%). RMN ^{1}H (400 MHz, DMSO-d_6) δ: 9,56 (s, 1H); 8,79 (s, 1H); 8,69 (s, 1H); 8,25 (d, 1H, J = 4 Hz); 7,91 (dd, 1H, J = 1,6, 4 Hz); 7,84 (t, 1H, J = 8 Hz); 7,80-7,70 (m, 2H); 7,61-7,50 (m, 5H); 7,38-7,30 (m, 2H); 7,25 (a s, 1H); 6,85 (s, 1H); 4,76 (d, 2H, J = 4 Hz); 4,35 (s, 2H); 2,98 (s, 3H). CLEM Procedimiento T: tiempo de retención 1,52 min, [M+1] = 497,2; HPLC Procedimiento A1: pureza 98,5 %, tiempo de retención = 6,42 min.

EJEMPLO 209

5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)isoxazol-3-carboxilato de etilo

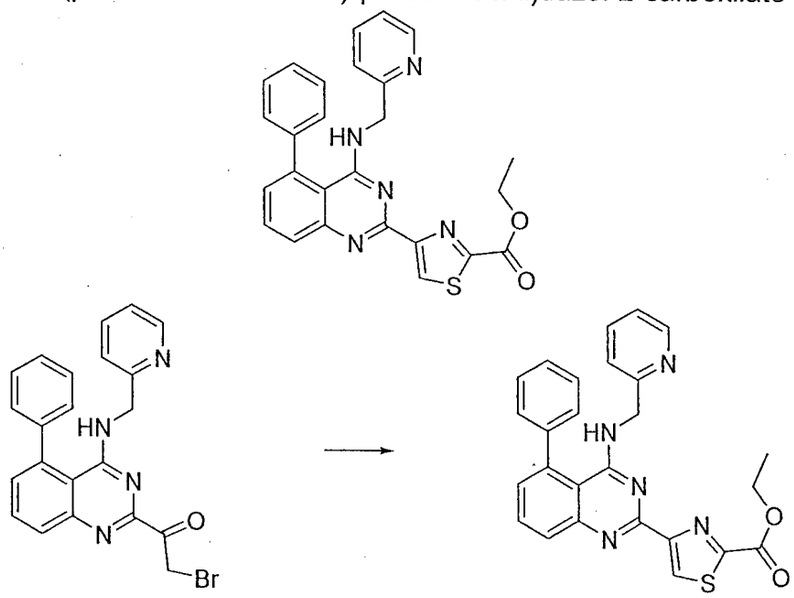




Una solución de 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)-4,5-dihidroisoxazol-3-carboxilato de etilo (del ejemplo 215, véase el procedimiento descrito más adelante, 0,30 g, 0,66 mmol), DDQ (0,06 g, 0,3 mmol) en tolueno (15 ml) se calentó a 75ºC durante 16 horas. Después de este tiempo, la mezcla de reacción se concentró a presión reducida y el residuo resultante se purificó mediante cromatografía ISCO (40% de acetato de etilo en hexanos) obteniendo el ejemplo 209 (0,075 g, rendimiento del 25%) en forma de un sólido blancuzco. RMN ^{1}H (400 MHz, DMSO-d_6) δ: 8,30 (s, 1H); 8,21 (s, 1H); 7,99-7,87 (m, 3H); 7,73 (dt, 1H, J = 1,6, 7,6 Hz); 7,63-7,48 (m, 6H); 7,40-7,32 (m, 2H); 7,24 (dd, 1H, J = 5,6, 7,2 Hz); 7,03 (a s, 1H); 4,71 (d, 2H, J = 4 Hz). CLEM Procedimiento T: tiempo de retención 1,81 min, [M+1] = 423,2; HPLC Procedimiento A1: pureza 99,3 %, tiempo de retención = 7,31 min.

EJEMPLO 210

4-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)tiazol-2-carboxilato de etilo

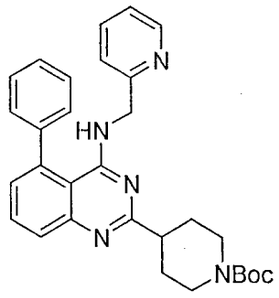


El compuesto 2-bromo-1-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)etanona (del ejemplo 203: 0,5 g, 1 mmol) se disolvió en etanol (20 ml) y se añadió tiooxamato de etilo (0,15 g, 1,2 mmol). La mezcla de reacción se agitó a 70ºC durante 1 hora. El etanol se evaporó a presión reducida y el residuo resultante se disolvió en DCM (25 ml). La porción orgánica se lavó con solución al 10% de bicarbonato sódico y la capa acuosa se extrajo con DCm (2 x 20 ml). Las fases orgánicas combinadas se secaron y se evaporaron a presión reducida. El residuo resultante se purificó mediante cromatografía ISCO (30% de acetato de etilo en hexanos) dando el Ejemplo 210 (0,13 g, rendimiento del 24%). RMN ^{1}H (400 MHz, DMSO-d_6) δ: 8,94 (s, 1H); 8,24 (d, 1H, J = 4 Hz); 7,96 (d, 1H, J = 8,8 Hz); 7,87 (t, 1H, J = 8 Hz); 7,74 (t, 1H, J = 8 Hz); 7,50-7,60 (m, 5H); 7,30-7,36 (m, 2H); 7,25 (t, 1H, J = 6 Hz); 6,95 (a s, 1H); 4,75 (d, 2H, J = 4 Hz); 4,47 (c, 2H, J = 7,2 Hz); 1,41 (t, 3H, J = 7,2 Hz).

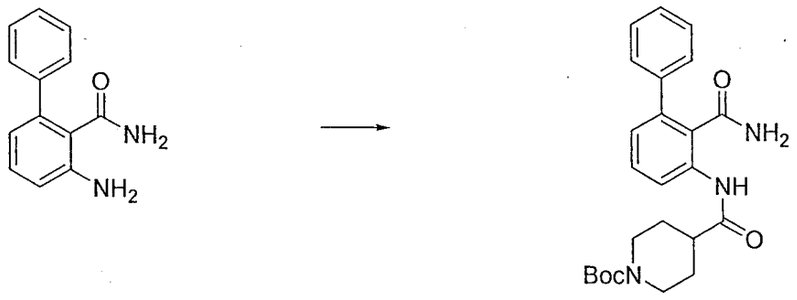
CLEM Procedimiento W: tiempo de retención 2,243 min, [M+1] = 468,2. HPLC Procedimiento A1: pureza 94,4 %, tiempo de retención = 7,522 min.

EJEMPLO 211

4-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piperidin-1-carboxilato de terc-butilo



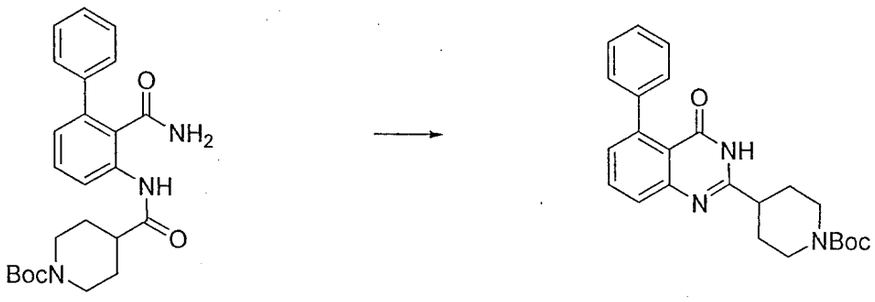
Etapa 1. Preparación de 4-(2-carbamoilbifenil-3-ilcarbamoil)piperidin-1-carboxilato de terc-butilo



A una solución de ácido 1-(terc-butoxicarbonil)piperidin-4-carboxílico (2,4 g, 10 mmol) en DCM (40 ml) se añadió HATU (5,3 g, 14 mmol) y DIPEA (3,6 ml, 28 mmol) y la mezcla de reacción se agitó a temperatura ambiente durante 1 hora. Se añadió 3-aminobifenil-2-carboxamida (del ejemplo 218)

(1,5 g, 7,07 mmol) y la mezcla resultante se agitó durante 16 horas adicionales. La mezcla de reacción se lavó con agua, la porción orgánica se secó, se filtró y se concentró a presión reducida. El residuo resultante se purificó mediante cromatografía ISCO (50% de acetato de etilo en hexanos) dando 4-(2-carbamoilbifenil-3-ilcarbamoil)piperidin-1-carboxilato de terc-butilo (1,0 g, rendimiento del 22%) en forma de un sólido blanco. CLEM Procedimiento T: tiempo de retención 1,71 min [M+1] = 423,0.

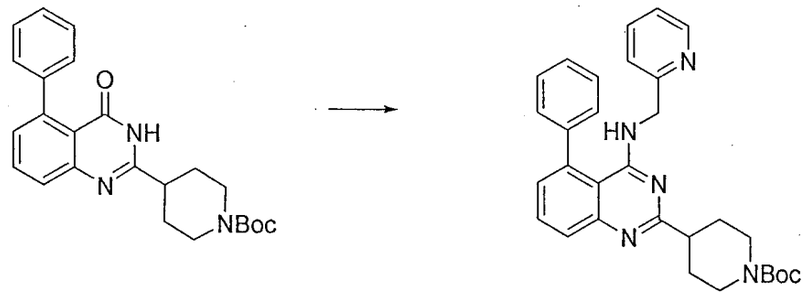
Etapa 2. Preparación de 4-(4-oxo-5-fenil-3,4-dihidroquinazolin-2-il)piperidin-1-carboxilato de terc-butilo



A una solución de 4-(2-carbamoilbifenil-3-ilcarbamoil)piperidin-1-carboxilato de terc-butilo (1.0 g, 2.4 mmol) en metanol se añadió NaOMe (2,6 ml, 25% en MeOH, 12,3 mmol). La mezcla de reacción resultante se agitó a temperatura ambiente durante 14 horas. Después de este tiempo, la mezcla de reacción se concentró a presión reducida y el residuo resultante se diluyó con acetato de etilo y después se lavó con agua. La porción orgánica se secó, se concentró a presión reducida, dando un residuo. El residuo resultante se purificó mediante cromatografía ISCO (30% de EtOAc en hexanos) dando 4-(4-oxo-5-fenil-3,4-dihidroquinazolin-2-il)piperidin-1-

carboxilato de terc-butilo (0,60 g, rendimiento del 67 %) en forma de un sólido blanco. CLEM Procedimiento W: tiempo de retención 2,07 min [M+1] = 422,2.

Etapa 3. Ejemplo 211



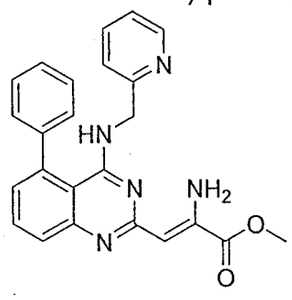
A una solución de 4-(4-oxo-5-fenil-3,4-dihidroquinazolin-2-il)piperidin-1-carboxilato de terc-butilo (0,6 g, 1 mmol) en acetonitrilo (20 ml) a temperatura ambiente se añadió DBU (0,45 g, 2,96 mmol) y BOP (0,98 g, 2,22 mmol). La mezcla de reacción se agitó durante 30 minutos y después se añadió aminometilpiridina (0,24 g, 2,22 mmol). La solución resultante se agitó durante 16 horas adicionales. La mezcla de reacción se concentró después a presión reducida y el residuo resultante se purificó mediante cromatografía en gel de sílice (20% de EtOAc en hexanos) proporcionando el ejemplo 211 (0,32 g, rendimiento del 45%) en forma de un sólido blanco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,20 (as, 1H); 7,86-7,68 (m, 3H); 7,60-7,52 (m, 5H), 7,32-7,17 (m, 3H), 6,64 (a , 1H), 4,60 (a s, 2H), 4,04 (a d, 2H, J = 8,8 Hz), 3,03-2,79 (a m, 3H), 1,94 (a t, 2H, J = 13,6 Hz), 1,72 (dd, 2H, J = 11,2 Hz, J = 20 Hz), 1,43 (s, 9H).

CLEM Procedimiento W: tiempo de retención 1,80 min, [M+1] = 475,2. HPLC

Procedimiento A1: pureza 97,4 %, tiempo de retención = 8,08 min.

EJEMPLO 212

2-amino-3-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)acrilato de (Z)-metilo

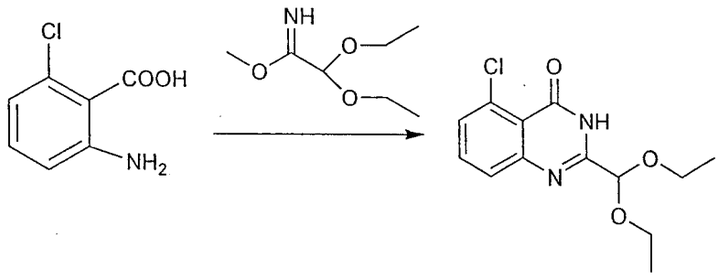


Etapa 1. Preparación de 2,2-dietoxiacetamida de metilo



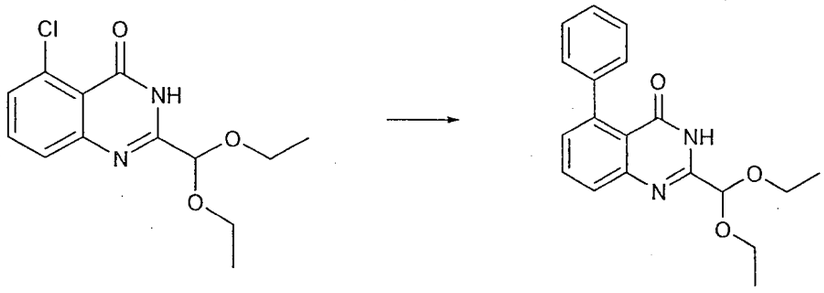
A una solución agitada de dietoxiacetonitrilo (5 g, 38,75 mmol) en metanol seco (80 ml) se añadió 1 ml de una solución al 20% de metóxido sódico. Después de la adición, la mezcla de reacción se agitó a temperatura ambiente durante 24 horas, se inactivó con CO_2 sólido y después se concentró. El residuo resultante se diluyó con agua y se extrajo con cloroformo. La capa orgánica se lavó con salmuera y se secó sobre Na_2SO_4 dando 2,2-dietoxiacetimidato de metilo (6 g, 96%). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 7,95 (s, 1H),) , 4,82 (s, 1H), 3,66 (s, 3H), 3,49 (c , 4H, J = 7,2 Hz); 1,16-1,13 (t, , 3H, J = 7,2 Hz).

Etapa 2. Preparación de 5-cloro-2-(dietoximetil)quinazolin-4(3H)-ona



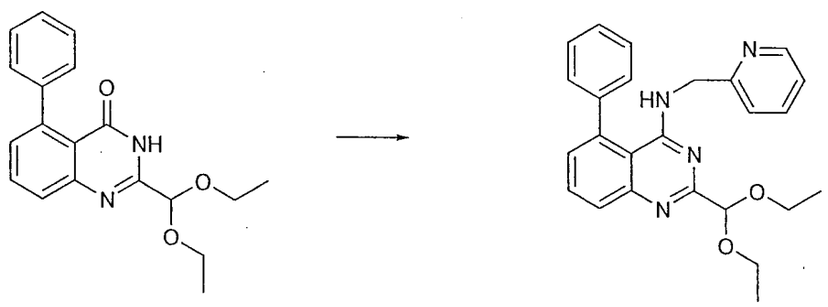
A una solución agitada de ácido 6-cloro-antranílico (6 g, 34,97 mmol) en EtOH (60 ml) en atmósfera de nitrógeno se añadió 1,5 equivalentes de TEA (¡4 ml, 104,9 mmol). Tras finalizar la adición, la mezcla se calentó hasta 50ºC, temperatura a la que se agitó durante 30 minutos. Después de este tiempo se añadió 2,2-dietoxiacetimidato de metilo (6 g, 41,96 mmol) en solución de etanol a través de una jeringuilla y la mezcla resultante se calentó hasta reflujo, momento en el que se agitó durante 24 horas. Al finalizar este periodo, la mezcla de reacción se enfrió hasta la temperatura ambiente y se evaporaron los volátiles. El residuo resultante se diluyó en agua, se extrajo con DCM y se lavó con solución de salmuera. El producto bruto se purificó mediante cromatografía en columna (25% de acetato de etilo en hexano) proporcionando 5-cloro-2-(dietoximetil)quinazolin-4(3H)-ona (7 g, rendimiento del 60%). CLEM Procedimiento W: tiempo de retención 1,5 min [M+1] = 283.

Etapa 3. Preparación de 2-(dietoximetil)-5-fenilquinozolina-4(3H)ona



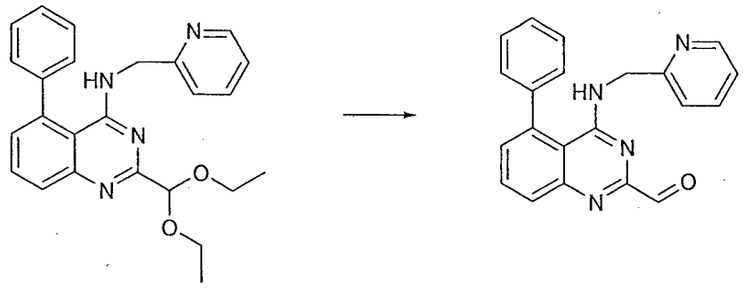
A una solución de 5-cloro-2-(dietoximetil)quinozolin-4(3H)-ona (5 g, 17,68 mmol) en una mezcla de dioxano-agua (45:15 ml) se añadió ácido fenilborónico (2,8 g, 22,9 mmol) y carbonato potásico (7,32 g, 53.05 mmol). La mezcla de reacción se desgasificó con nitrógeno durante 30 minutos y después se añadió tetraquistrifenilfosfina paladio (2,04 g, 1,76 mmol). La mezcla resultante se calentó hasta reflujo, momento en el que se agitó durante 24 horas. Al finalizar este periodo, la mezcla de reacción se enfrió hasta la temperatura ambiente, se concentró y después se diluyó con agua. La mezcla resultante se filtró a través de celite, se lavó con DCM y después se extrajo con DCM. La capa orgánica se secó sobre Na_2SO_4, se diluyó con acetato de etilo, se lavó con agua y salmuera, y después se secó sobre Na_2SO_4 El producto bruto se purificó mediante cromatografía en gel de sílice (25% de acetato de etilo en hexano) proporcionando 2-(dietoximetil)-5-fenilquinazolin-4(3H)-ona (4,5 g, rendimiento del 78 %). CLEM Procedimiento V: tiempo de retención 1,62 min [M+1] = 325,0.

Etapa 4. Preparación de 2-(dietoximetil)-5-fenil-N-(piridinil-2-metil)quinazolin-4-amina



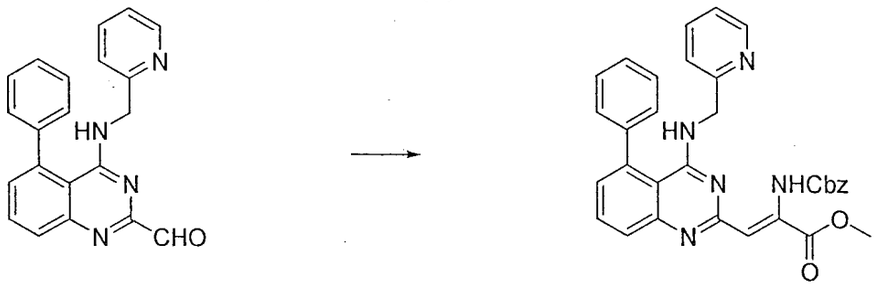
A una solución de 2-(dietoximetil)-5-fenilquinozolin-4(3H)ona (5 g, 15,4 mmol) en acetonitrilo (50 ml) en atmósfera de nitrógeno se añadió reactivo BOP (10,25 g, 23,12 mmol) seguido por DBU (6,3 ml, 46,2 mmol). La mezcla de reacción se agitó a temperatura ambiente durante una hora y después se añadió una solución de 2-aminometilpiridina (2,5 ml, 23,12 mmol) en acetonitrilo. La mezcla resultante se agitó a temperatura ambiente en nitrógeno durante 20 horas. Después de este tiempo, la solución se concentró a presión reducida y se diluyó con agua. La solución acuosa se extrajo con acetato de etilo y después se lavó con solución de salmuera. El producto bruto se purificó usando cromatografía en gel de sílice (23 % de acetato de etilo en hexano) proporcionando 2-(dietoximetil)-5-fenil-N-(piridinil-2-metil)quinozolin-4-amina (3,3 g, 52 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,21- (s, 1H), 7,80-7,75 (m, 2H), 7,72-7,19 (m, 1H), 7,55-747 (m, 5H), 7,29-7,21 (m, 3H), 6,72 (s, 1H), 5,33 (s, 1H), 4,58 (d, 2H, J = 4 Hz); 3,77-3,60 (m, 4H), 1,17-1,13 (t, 6H, J = 6,8 Hz). CLEM Procedimiento V: tiempo de retención 1,69 min [M+1] = 415,0.

Etapa 5. Preparación de 5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-carbaldehído



A una solución de 2-(dietoximetil)-5-fenil-N-(piridinil-2-metil)quinozolin-4-amina (3 g, 7,24 mmol) en 1,4-dioxano (30 ml) en atmósfera de nitrógeno se añadió HCl (30 ml, 6M). La mezcla resultante se calentó a 90°C durante 4 horas. Después de este tiempo, la mezcla se enfrió hasta la temperatura ambiente y después se concentró a presión reducida. Esta mezcla se diluyó con agua, se neutralizó con Na_2CO_3 sólido y después se extrajo con DCM. La capa orgánica se secó son sulfato sódico y se evaporó a presión reducida dando 5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-carbaldehído (1,5 g, 42 %). CLEM Procedimiento V: tiempo de retención 1,70 min [M+1] = 340,0.

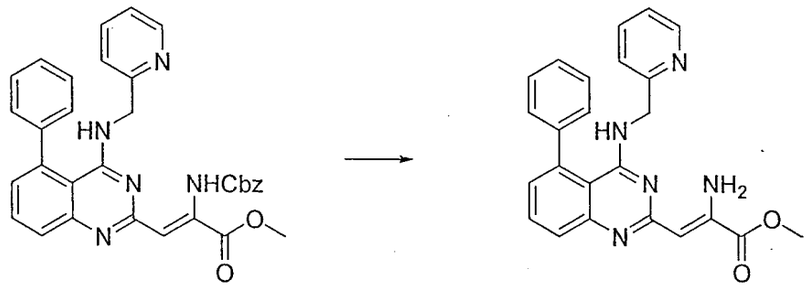
Etapa 6. Preparación de 2-(benciloxicarbonilamino)-3-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)acrilato de (Z)-metilo



A una solución de 5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-carbaldehído (0,9 g, 3 mmol) en THF (10 ml) se añadió 2-benciloxicarbonilamino-2(dimetoxifosfinil)acetato de metilo (0,96 g, 2,9 mmol) seguido por tetrametilguanidina (0,66 ml, 5,3 mmol). La solución resultante se agitó a temperatura ambiente durante 3 horas. Después de este tiempo, la mezcla de reacción se diluyó con acetato de etilo, se lavó sucesivamente con agua y salmuera, se secó sobre Na_2SO_4, se filtró y se concentró a presión

reducida. El residuo resultante se purificó mediante cromatografía en gel de sílice (acetato de etilo 30% en hexano) dando 2-(benciloxicarbonilamino)-3-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)acrilato de (Z)-metilo (0,7 g (rendimiento del 48 %). CLEM Procedimiento V: tiempo de retención 1,94 min [M+1] = 546,0.

Etapa 7. Ejemplo 212

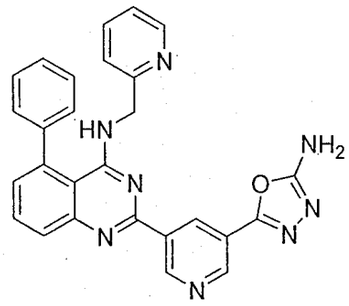


A una solución de 2-(benciloxicarbonilamino)-3-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)acrilato de (Z)-etilo (0,4 g, 0,7 mmol) en MeOH (7 ml) se añadió 10% de paladio sobre carbono (40 mg). Tras finalizar la adición, la mezcla de reacción se agitó a temperatura ambiente en atmósfera de hidrógeno durante 20 horas. Después de este tiempo, la mezcla de reacción se filtró a través de celite y el filtrado se evaporó a presión reducida. El residuo resultante se purificó mediante cromatografía en gel de sílice (23 % de acetato de etilo en hexano) dando el Ejemplo 212 (0,3 g, rendimiento del 88 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,21 (d, 1H, J = 4,4Hz); 7,72-7,68 (m, 3H), 7,54-7,45 (m, 5H), 7,25-7,21 (m, 2H), 7,14 (d, 1H, J = 6 Hz); 5,97(s, 1H), 4,55 (d, 2H, J = 2,8 Hz), 3,84 (s,1H). CLEM Procedimiento V: tiempo de retención 1,74 min, [M+1] = 412,0; HPLC Procedimiento A2: pureza 97,7 %, tiempo de retención = 8,90 min.

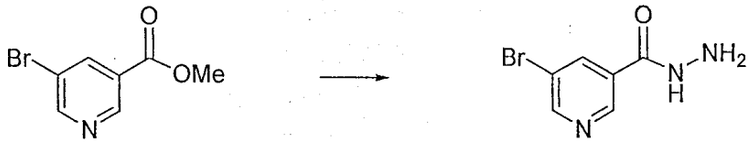
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EJEMPLO 213

5-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)-1,3,4-oxadiazol-2-amina

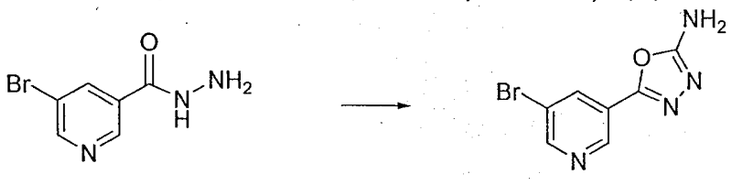


Etapa 1. Preparación de 5-bromonicotinohidrazida



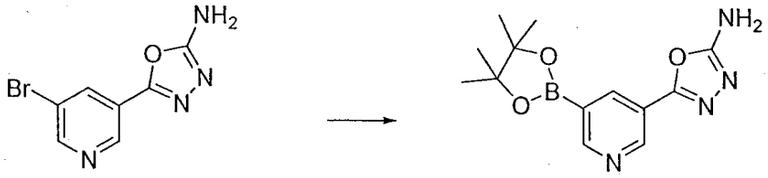
A una solución de 5-bromonicotinato de metilo (5 g, 23 mmol) en etanol (40 ml) se añadió hidrato de hidracina (6 ml, 115 mmol). La mezcla de reacción se sometió a reflujo a 90ºC durante 4 horas. Después de este tiempo, la mezcla de reacción se evaporó hasta sequedad y después se redisolvió en acetato de etilo. La capa orgánica se lavó con agua, se secó y se evaporó dando 5-bromonicotinohidrazida (3,4 g, 72 %). CLEM Procedimiento T: tiempo de retención 0,573 min [M+1] = 216,0, 218,0.

Etapa 2. Preparación de 5-(5-bromopiridin-3-il)-1,3,4-oxadiazol-2-amina



A una solución de 5-bromonicotinohidracida (2 g, 9 mmol) en dioxano (48 mmol) se añadió bicarbonato sódico (0,78 g, 9,2 mmol) y 20 ml de agua. La mezcla de reacción se dejó agitar durante 10 minutos y después se añadió bromuro de cinógeno (1,17g, 10 mmol). La solución transparente resultante se dejó agitar durante la noche a temperatura ambiente. Al finalizar este periodo, se recogió un precipitado rosado mediante filtración, dando 5-(5-bromopiridin-3-il)-1,3,4-oxadiazol-2-amina (3,4 g, rendimiento del 72 %). CLEM Procedimiento Y: tiempo de retención 1,43 min [M+1] = 239,0, 241,0.

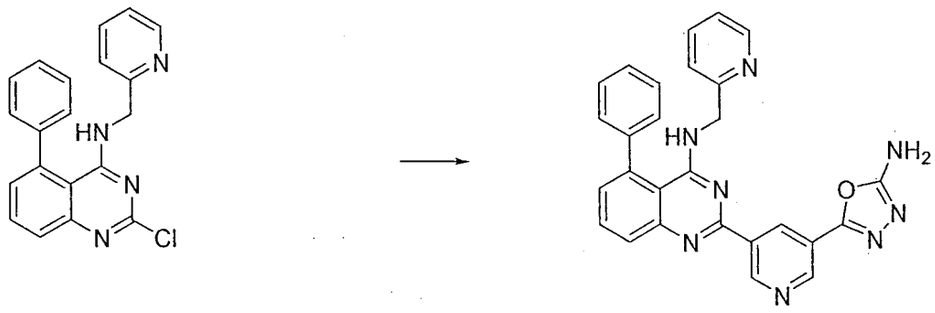
Etapa 3. Preparación de 5-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-piridin-3-il)-1,3,4-oxadiazol-2-amina



Una mezcla de 5-(5-bromopiridin-3-il)-1,3,4-oxadiazol-2-amina (0,2 g, 0,8 mmol), bis(pinacolato)diboro (0,28 g, 1,0 mmol) y acetato potásico (0,25 g, 2,5 mmol) en 1,4-dioxano (8 ml) se desgasificó con nitrógeno durante 15 minutos. Después de este tiempo se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio(II) diclorometano (0,055 g, 0,06 mmol) y la mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se calentó después en un reactor microondas a 120ºC, durante 45 minutos. Al finalizar este periodo, la mezcla de reacción se filtró a través de celite y el filtrado se concentró a presión reducida proporcionando 5-(5-((4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-il)-1,3,4-oxadioazol-2-amina bruta (0,3 g), que se usó sin

purificación adicional.

Etapa 4. Ejemplo 213

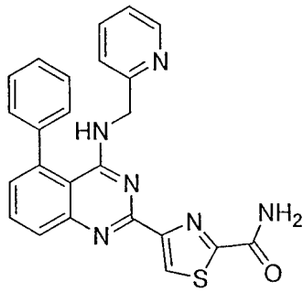


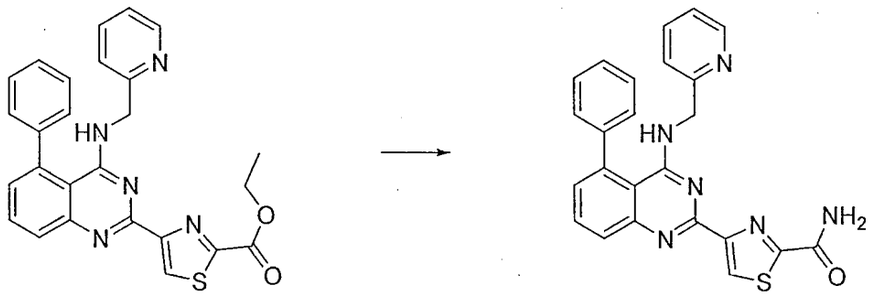
A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (del ejemplo 1, etapa 4, 0,2 g, 0,5 mmol) en 1,4-dioxano (8 ml) y H_2O (0,55 ml) en nitrógeno se añadió 5-(5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-il)-1,3,4-oxadiazol-2-amina (0,2 g, 0,7 mmol), y carbonato potásico (0,24 g, 1,7 mmol). La mezcla de reacción se desgasificó con nitrógeno durante 15 minutos. Después de este tiempo, se añadió el complejo cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (0,047 g, 0,050 mmol) y la mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. Al finalizar este periodo, la mezcla de reacción se agitó a 90°C durante 16 horas y después se dejó enfriar hasta la temperatura ambiente. Una vez a la temperatura prescrita, la mezcla de reacción se inactivó mediante la adición de agua. La mezcla de reacción se transfirió después a un embudo de separación y la capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El residuo resultante se purificó mediante cromatografía en columna en gel de

sílice (5% metanol en diclorometano), dando el Ejemplo 213 (0,067 g, rendimiento del 10 %) en forma de un sólido blanco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,71 (s, 1H); 9,11 (s, 2H); 8,25-8,23 (m, 1H0; 7,92 (d, 1H< J = 8Hz); 7,86 (t, 1H, J = 8 Hz); 7, 73 (t, 1H, J = 8 Hz); 7,60-7,50 (m, 5H), 7,46 (a s, 2H); 7,37-7,31 (m, 2H); 7,22 (t, 1H, J = 4 Hz); 6,93 (as, 1H); 4,76 (d, 2H, J = 4 Hz). CLEM Procedimiento W: tiempo de retención 1,80 min, [M+1] = 473,2; HPLC Procedimiento A4: pureza 95,9 %, tiempo de retención = 6,11 min.

EJEMPLO 214

4-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)tiazol-2-carboxamida



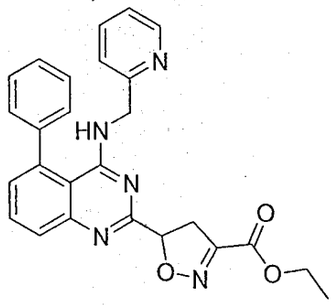


Una solución de 4-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)tiazol-2-carboxilato de etilo (del ejemplo 210, 90 mg, 0,19 mmol) en NH_3 (2,0 M en

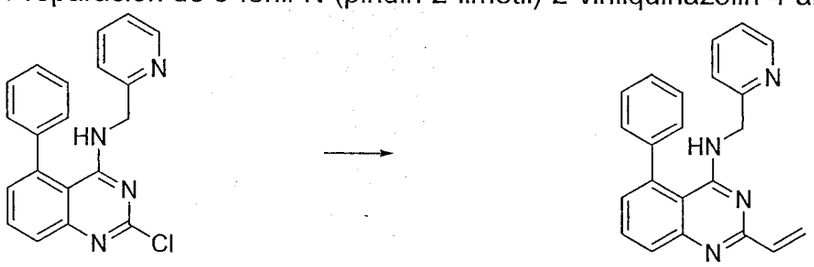
MeOH, 5 ml) se agitó a temperatura ambiente en un vaso sellado durante 30 minutos. El sólido formado se filtró y se lavó con metanol enfriado con hielo. El sólido se purificó después mediante HPLC preparativa (Procedimiento S) proporcionando el Ejemplo 214 (35 mg, rendimiento del 42%). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,79 (s, 1H); 8,26 (s, 1H); 8,22 (s, 1H); 7,97 (a s, 1H); 7,90-7,81 (m, 2H); 7,73 (dt, 1H, *J* = 2, 7,6 Hz); 7,61-7,49 (m, 5H); 7,32-7,30 (m, 2H); 7,26-7,20 (m, 1H); 6,77 (t, 1H, *J* = 4,8 Hz); 4,73 (d, 2H, *J* = 4,8 Hz). CLEM Procedimiento W: tiempo de retención 1,85 min, [M+1] = 439,2; HPLC Procedimiento A1: Pureza del 95,2 %, tiempo de retención = 6,26 minutos. HPLC preparativa Procedimiento: S.

EJEMPLO 215

1-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)-4,5-dihidroisoxazol-3-il)butan-1-ona



Etapa 1. Preparación de 5-fenil-N-(piridin-2-ilmetil)-2-vinilquinazolin-4-amina



A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,5 g, 1,44 mmol) en 1,4-dioxano (10 ml) se añadió $Pd(TPP)_2Cl_2$ (0,101 g, 0,144 mmol) y tributilvinilestaño (2,285 g, 7,20 mmol) en una corriente de nitrógeno. Tras finalizar la adición, la mezcla de reacción se calentó hasta reflujo a 90ºC durante 16 horas. Después de este tiempo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente y después se concentró a presión reducida. El residuo resultante se purificó mediante cromatografía en columna en gel de sílice (20% de acetato de etilo, hexano) dando 5-fenil-N-(piridin-2-ilmetil)-2-vinilquinazolin-4-amina (0,38 g, rendimiento del 78 %) en forma de un sólido blanco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,22 (dd, 1H, *J* = 4,8Hz), 7,76 (d, 1H, *J* = 1,6 Hz), 7,75 (s, 1H), 7,70 (dt, 1H, *J* = 2 Hz, 8 Hz), 7,45-7,56 (m, 5H), 7,20-7,28 (m, 3H), 6,72 (dd, 1H, *J* = 10,4 Hz, 17,2 Hz), 6,64 (t, 1H, *J* = 3,6 Hz), 6,56 (dd, 1H, *J* = 1,6 Hz, 17,2 Hz), 5,67 (d, 1H, *J* = 10,4 Hz), 4,62 (d, 2H, *J* = 4,0 Hz). CLEM Procedimiento T: tiempo de retención 1,500 min, [M+1] = 339,2; HPLC Procedimiento A2: pureza 98,1 %, tiempo de retención = 8,74 min.

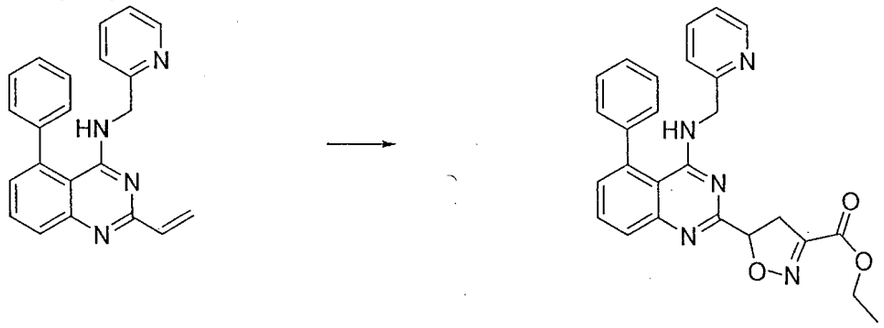
Etapa 2. Preparación de 2-cloro-2-(hidroxiimino)acetato de (Z)-etilo



A una solución de clorhidrato de éster de glicina (2 g, 14 mmol) en 3 ml de agua se añadió HCl concentrado (1,2 ml). Tras finalizar la adición, la solución resultante se enfrió hasta -5ºC y después se añadió una solución de nitrito sódico (1 g, 14 mmol) en agua (1,4 ml). La mezcla resultante se agitó a

0ºC durante 10 minutos y después se añadió otra solución de nitrito sódico (1 g, 14 mmol) en agua (1,4 ml). La mezcla resultante se agitó a 0ºC durante 45 minutos. Al finalizar este periodo se añadió una solución de salmuera. La mezcla de reacción se extrajo con éter, se secó y s evaporó a presión reducida dando 2-cloro-2-(hidroxiimino)acetato de (Z)-etilo (1,6 g, 76 %), que se pasó a la siguiente etapa inmediatamente sin purificación adicional.

Etapa 3. Ejemplo 215

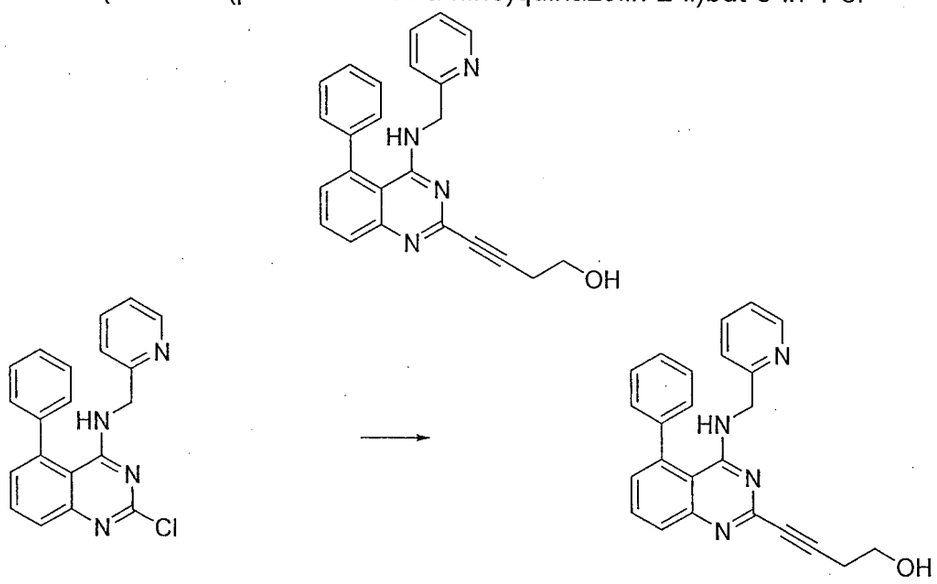


Una solución de 5-fenil-N-(piridin-2-ilmetil)-2-viniquinazolin-4-amina (0,4 g, 1 mmol), 2-cloro-2-(hidroxiimino)acetato de (Z)-etilo (0,534 g, 3,54 mmol) y trietilamina (0,358 g, 3,54 mmol) en DCM (10 ml) se agitó a temperatura ambiente durante 16 horas. Después de este tiempo, la mezcla de reacción se concentró a presión reducida dando un residuo. El residuo resultante se purificó mediante cromatografía ISCO (30 % de acetato de etilo en hexano), dando el Ejemplo 215 (0,2 g, rendimiento del 38 %) en forma de un sólido blancuzco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,21 (d, 1H, J = 4 Hz), 7,88-7,80 (m, 2H), 7,68 (dd, 1H, J = 1,6 Hz, 8,0 Hz), 7,60-7,47 (m, 5H), 7,32 (dd, 1H, J = 2,4, 6,0 Hz), 7,25-7,20 (m, 2H), 6,78 (as, 1H), 5,74 (dd, 1H, J = 8, 12 Hz), 4,54 (dd, 2H, J = 4, 6,8 Hz), 4,31 (c, 2H, J = 8,0 Hz), 3,73 (dd, 1H, J = 8, 17,6 Hz), 3,60 (dd, 1H, J = 5,6, 17,2 Hz), 1,30 (t, 3H, J = 7,2 Hz). CLEM

Procedimiento W: tiempo de retención 2,033 min, [M+1] = 454,4; HPLC Procedimiento A2: pureza 95,1 %, tiempo de retención = 8,65 min.

EJEMPLO 216

4-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)but-3-in-1-ol

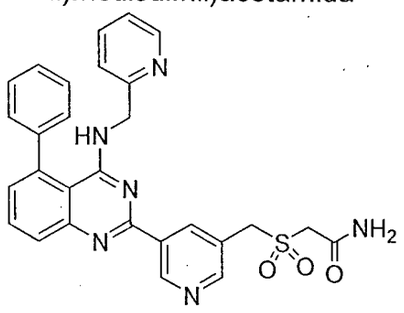


Una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (del ejemplo 1, etapa 4, 0,3 g, 0,9 mmol) y alcohol homopropargílico (0,07 ml, 1 mmol) en acetonitrilo (10 ml) se desgasificó con nitrógeno y después se añadieron $Pd(TPP)_2Cl_2$ (0,060 g, 0,085 mmol), trietilamina (0,4 ml, 4 mmol) y CuI (0,016 g, 0,080 mmol). La mezcla de reacción se calentó a 60ºC durante 16 horas. Después de este tiempo, la mezcla de reacción se filtró a través de celite. El filtrado resultante se diluyó con acetato de etilo y después se lavó sucesivamente con agua y salmuera. La capa orgánica se secó, se filtró y se concentró a presión reducida, dando un residuo. El residuo resultante se purificó mediante cromatografía en gel de sílice (2 % de metanol en hexanos),

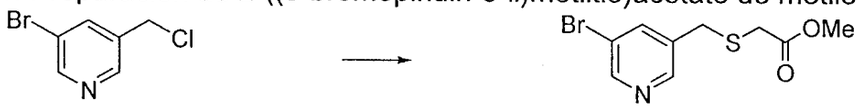
dando el Ejemplo 216 (0,15 g, rendimiento del 46 %) en forma de un sólido blancuzco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,18 (a s, 1H); 7,88 (t, 1H, J = 8 Hz); 7,77-7,72 (m, 2H); 7,60-7,48 (m, 5H); 7,38-7,30 (m, 3H); 7,26-7,22 (m 1H); 4,62 (d, 2H, J = 4 Hz); 3,66 (t, 2H, 6,8 Hz); 2,67 (t, 2H, J = 6,8 Hz). CLEM Procedimiento W: tiempo de retención 1,72 min, [M+1] = 381,2; HPLC Procedimiento A1: pureza 98,5 %, tiempo de retención = 6,03 min.

EJEMPLO 217

2-((5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piridin-3-il)metilsulfnil)acetamida



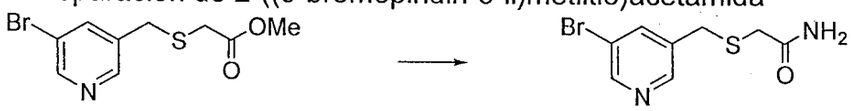
Etapa 1. Preparación de 2-((5-bromopiridin-3-il)metiltio)acetato de metilo



A una solución de 3-bromo-5-(clorometil)piridina (del ejemplo 199 (1,2 g, 5,8 mmol) en acetonitrilo (15 ml) se añadió K_2CO_3 (0,97 g, 7,0 mmol) seguido por 2-mercaptoacetato de metilo (0,57 ml, 6,4 mmol). La solución resultante se agitó a temperatura ambiente durante 16 horas. Después de este tiempo, la mezcla de reacción se filtró y el filtrado se diluyó con acetato de etilo y se

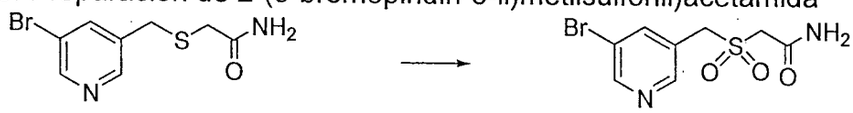
lavó con agua. La porción orgánica se secó, se filtró y se concentró a presión reducida. El residuo resultante se purificó mediante cromatografía en gel de sílice (30 % de acetato de etilo en hexano) proporcionando 2-((5-bromopiridin-3-il)metiltio) acetato de metilo (1,2 g, rendimiento del 80 %). CLEM Procedimiento Y: tiempo de retención 1,66 min [M+1] = 276,0.

Etapa 2. Preparación de 2-((5-bromopiridin-3-il)metiltio)acetamida



Una solución de 2-((5-bromopiridin-3-il)metiltio)acetato de metilo (1,2 g, 4,5 mmol) en NH_3 (2,0 M en MeOH, 40 ml) se calentó a 80ºC en un vaso sellado durante 2 horas. Después de este tiempo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiental y, después, el disolvente se evaporó a presión reducida. El residuo resultante se recristalizó en EtOAc/hexanos proporcionando 2-((5-bromopiridin-3-il)metiltio)acetamida (0,8 g, rendimiento del 72 %) CLEM Procedimiento W: tiempo de retención 1,08 min [M+1] = 263,0.

Etapa 3. Preparación de 2-(5-bromopiridin-3-il)metilsulfonil)acetamida

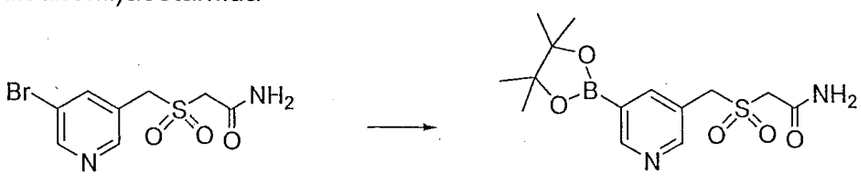


A una solución de 2-((5-bromopiridin-3-il)metiltio)acetamida (0,8 g, 3,0 mmol) en MeOH:H_2O (30:10 ml) se añadió oxona® (2,5 g, 3,9 mmol). La mezcla de reacción resultante se agitó a temperatura ambiente durante 2 horas. Después de este tiempo, el disolvente se evaporó y el residuo

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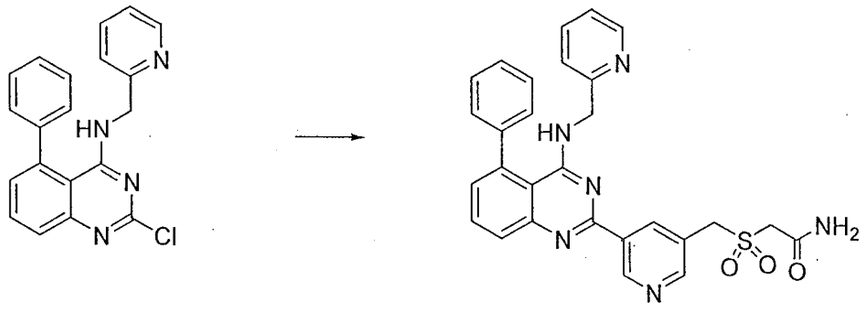
resultante se disolvió en EtOAc y se lavó con agua. La porción orgánica se concentró proporcionando 2-(5-bromopiridin-3-il)metilsulfonil)acetamida (0,6, 67%). CLEM Procedimiento T: tiempo de retención 0,68 min [M+1] = 293.

Etapa 4. Preparación de 2-((5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-piridin-3-il)metilsulfonil)acetamida



Una mezcla de 2-(5-bromopiridin-3-il)metilsulfonil)acetamida (10,3 g, 1,00 mmol), bis(pinacolato)diboro (0,337 g, 1,30 mmol) y acetato potásico (0,3 g, 3,0 mmol) en 1,4-dioxano (10 ml) se desgasificó con nitrógeno durante 15 minutos. Después de este tiempo se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio(II) diclorometano (0,066 mg, 0,08 mmol) y la mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno. La mezcla de reacción se calentó después en el reactor microondas a 120ºC, durante 45 minutos. Al finalizar este periodo, la mezcla de reacción se filtró a través de celite y el filtrado se concentró a presión reducida proporcionando 2((5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-il)metilsulfonil)acetamida (440 mg) en forma de un sólido marrón, que se usó sin purificación adicional.

Etapa 5. Ejemplo 217

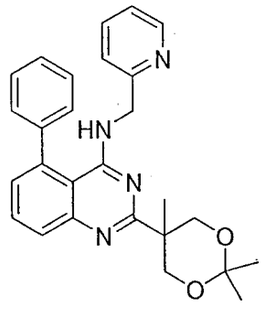


A una solución de 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (del ejemplo 1, etapa 4, 0,3 g, 0,9 mmol) en 1,4-dioxano (10 ml) y H_2O (2 ml) en nitrógeno se añadió 2-((5-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)piridin-3-il)metilsulfonil)acetamida (0,3 g, 0,9 mmol), y carbonato potásico (0,36 g, 2,6 mmol). La mezcla de reacción se desgasificó con nitrógeno durante 15 minutos y, después, se añadió el complejo de cloruro de (1,1'-bis(difenilfosfino)ferroceno)paladio (II) diclorometano (0,07 g, 0,08 mmol). La mezcla de reacción se desgasificó de nuevo durante 10 minutos con nitrógeno y después se agitó a 90ºC durante 16 horas. Al finalizar este periodo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente y después se inactivó mediante la adición de agua. La mezcla de reacción se transfirió a un embudo de separación y la capa acuosa se extrajo con acetato de etilo. Las porciones orgánicas combinadas se lavaron con agua y NaCl saturado, se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El concentrado resultante se purificó mediante TLC preparativa (5 % metanol en diclorometano), proporcionando el Ejemplo 217 (100 mg, rendimiento del 22 %) en forma de un sólido blancuzco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 9,62 (s, 1H); 9,84 (s, 1H); 8,84 (s, 1H); 8,23 (a s, 1H); 7,92-7,88 (m, 1H); 7,85 (t, 2H, J = 4Hz); 7,72 (t, 1H, J = 8Hz); 7,60-7,50 (m,

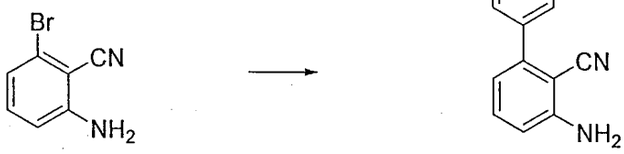
6H); 7,40-7,28 (m, 2H); 7,22 (t, 1H, *J* = 8Hz); 6,85 (a s, 1H); 4,85 (s, 2H); 4,73 (d, 2H, *J* = 4 HZ); 4,06 (s, 2H). CLEM Procedimiento W: tiempo de retención 1,70 min, [M+1] = 525,2; HPLC Procedimiento A2: pureza 99,5 %, tiempo de retención = 5,91 min.

EJEMPLO 218

5-fenil-N-(piridin-2-ilmetil)-2-(2,2,5-trimetil)-1,3-dioxan-5-il)quinazolin-4-amina



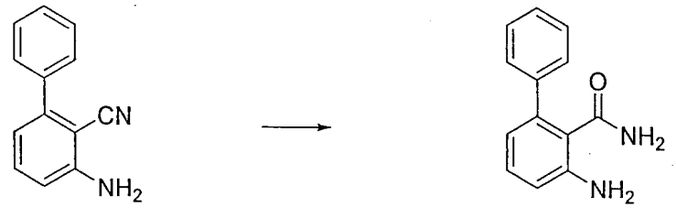
Etapa 1. Preparación de 3-aminobifenil-2-carbonitrilo



A una solución de 2-amino-6-bromobenzonitrilo (5 g, 0,025 mmol) en tolueno (70 ml) se añadió KOAc (5 g, 0,05 mmol), ácido fenilborónico (4,27 g, 0,035 mmol) y $Pd(TPP)_2Cl_2$ cat.. La mezcla de reacción se calentó hasta 115ºC durante 16 horas. Después de este tiempo, la mezcla de reacción se filtró y los volátiles se evaporaron dando un residuo. El residuo se purificó mediante cromatografía en columna (1% de EtOAc en hexanos),

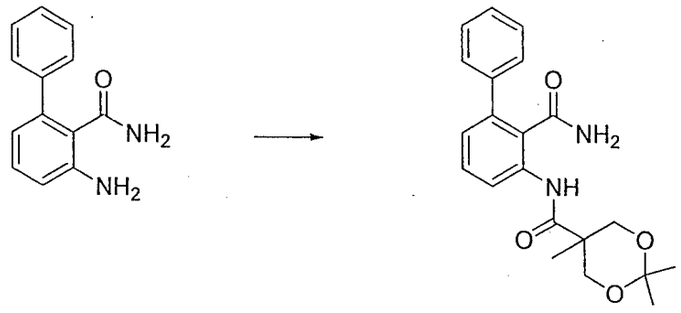
proporcionando 3-aminobifenil-2-carbonitrilo (3,2 g, rendimiento del 65%) en forma de un sólido amarillo claro. CLEM Procedimiento Z: tiempo de retención 3,65 min [M+] = 195,2

Etapa 2. Preparación de 3-aminobifenil-2-carboxamida



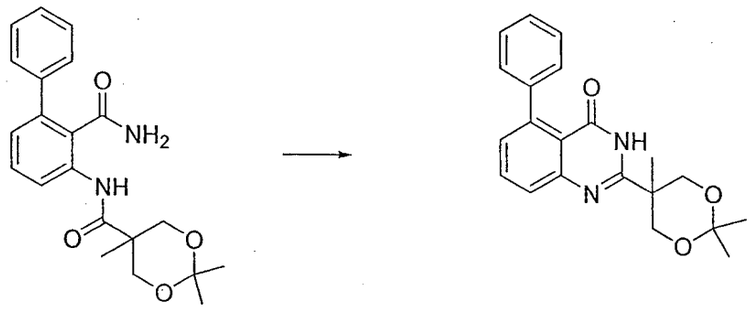
Una solución de 3-aminobifenil-2-carbonitrilo (4 g, 20 mmol) en etanol (20 ml) y NaOH acuoso (8 g, 200 mmol) se calentó a 100ºC en el reactor de microondas durante 1 hora 30 minutos. Después de este tiempo, el etanol se evaporó a presión reducida y el residuo resultante se extrajo con acetato de etilo. Los extractos orgánicos se concentraron a presión reducida, dando un residuo. El residuo se purificó mediante cromatografía en gel de sílice (50% de EtOAc en hexano) dando 3-aminobifenil-2-carboxamida (3,1 g, rendimiento del 72%) en forma de un sólido marrón. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 7,40-7,30 (m, 5H), 7,15 (a s, 1H), 7,11 (t, 1H, J = 8Hz), 6,72 (dd, 1H, J = 0,8, 8 Hz), 6,52 (dd, 1H, J =0,8, 8 Hz), 5,13 (s, 1H). CLEM Procedimiento W: tiempo de retención 1,28 min [M+1] = 213,0.

Etapa 3. Preparación de N-(2-carbamoilbifenil-3-il)-2,2,5-trimetil-1,3-dioxano-5-carboxamida



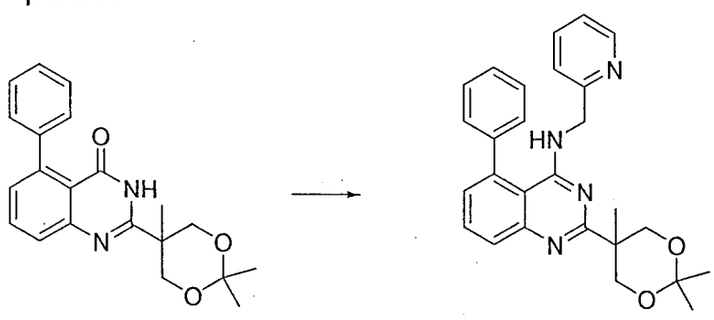
A una solución de ácido 2,2,5-trimetil-1,3-dioxano-5-carboxílico (0,6 g, 4 mmol) en DCM (30 ml) se añadió HTU (1,8 mg, 4,7 mmol) y DIPEA (1,6 ml, 23,5 mmol). La mezcla de reacción se agitó a temperatura ambiente durante 1 hora. Después de este tiempo se añadió 3-aminobifenil-2-carboxamida (0,6 g, 2,35 mmol) y la solución resultante se agitó durante 16 horas. Al finalizar este periodo, la mezcla de reacción se lavó con agua, se secó, se filtró y se concentró a presión reducida. El residuo resultante se purificó mediante cromatografía en gel de sílice (25% de acetato de etilo en hexanos) dando N-(2-carbamoilbifenil-3-il)-2,2,5-trimetil-1,3-dioxano-5-carboxamida (0,25 g, rendimiento del 24 %) en forma de un sólido blanco. CLEM Procedimiento Y: tiempo de retención 1,69 min [M+1] = 367,2.

Etapa 4. Preparación de 5-fenil-2-(2,2,5-trimetil-1,3-dioxan-5-il)quinazolin-4(3H)-ona



A una solución de N-(2-carbamoilbifenil-3-il)-2,2,5-trimetil-1,3-dioxano-5-carboxamida (0,23 g, 0,62 mmol) en metanol se añadió NaOMe (0,25 ml, 25% en MeOH, 1,2 mmol) y la mezcla de reacción se agitó a 50ºC durante 1 hora. Después de este tiempo, la mezcla de reacción se concentró y el residuo resultante se diluyó con acetato de etilo, después se lavó con agua. La porción orgánica se secó y se concentró a presión reducida, dando un residuo. El residuo resultante se purificó mediante cromatografía en gel de sílice (30 % de acetato de etilo en hexanos) dando 5-fenil-2-(2,2,5-trimetil-1,3-dioxan-5-il)quinazolin-4(3H)-ona (0,2 g, rendimiento del 91 %) pura en forma de un sólido blanco. RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 11,49 (a s, 1H), 7,77 (t, 1H, J = 8 Hz), 7,64 (d, 1H, J = 8 Hz), 7,36-7,28 (m, 5H), 7,21 (d, 1H, J = 8 Hz), 4,27 (d, 2H, J = 12 Hz), 3,91 (d, 2H, J = 12 Hz), 1,40 (s, 3H), 1,35 (d, 6H, 10,2 Hz). CLEM Procedimiento W: tiempo de retención 2,01 min [M+1] = 351.

Etapa 5. Ejemplo 218



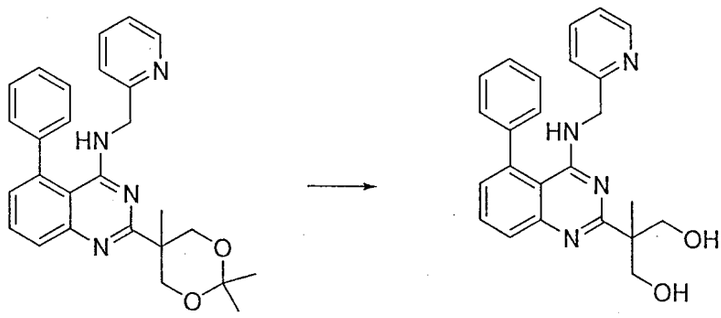
A una solución de 5-fenil-2-(2,2,5-trimetil-1,3-dioxan-5-il)quinazolin-4(3H)-ona (0,22 g, 0,62 mmol) en acetonitrilo (10 ml) a temperatura ambiente

000980

se añadió DBU (0,24 g, 1,57 mmol) y reactivo BOP (0,36 g, 0,81 mmol). La mezcla de reacción se agitó durante 30 minutos y después se añadió aminometilpiridina (0,11 ml, 0,11 mmol). La solución resultante se agitó durante 16 horas. Después de este tiempo, la mezcla de reacción se concentró a presión reducida y el residuo resultante se purificó mediante cromatografía en gel de sílice (30 % de EtOAc en hexanos) proporcionando el ejemplo 219 (0,18 g, rendimiento del 67 %) en forma de un sólido blanco. RMN ^{1}H (400 MHz, DMSO-d_6) δ: 8,26 (a s, 1H); 7,80-7,69 (m, 3H); 7,59-7,45 (m, 5H); 7,27-7,20 (m, 3H); 6,53 (a s, 1H); 4,55 (d, 2H, J = 4 Hz); 4,31 (d, 2H, J = 7,6 Hz); 3,79 (d, 2H, J = 7,6 Hz); 1,38 (d, 6H, J = 4,8 Hz); 1,33 (s, 3H). CLEM Procedimiento W: tiempo de retención 2,37 min, [M+1] = 441; HPLC Procedimiento A1: pureza 96,7 %, tiempo de retención = 6,87 min.

EJEMPLO 219

2-metil-2-(5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)propano-1,3-diol



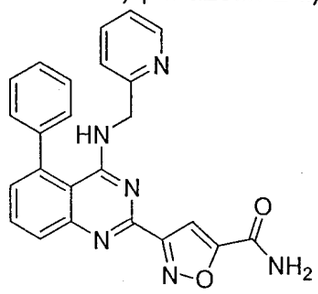
El compuesto 5-fenil-N-(piridin-2-ilmetil)-2-(2,2,5-trimetil)-1,3-dioxan-5-il)quinazolin-4-amina (del ejemplo 218, 0,1 g, 0,23 mmol) se disolvió en éter (2 ml). Tras la disolución, se añadió HCl M en éter (5 ml) y la mezcla

000981

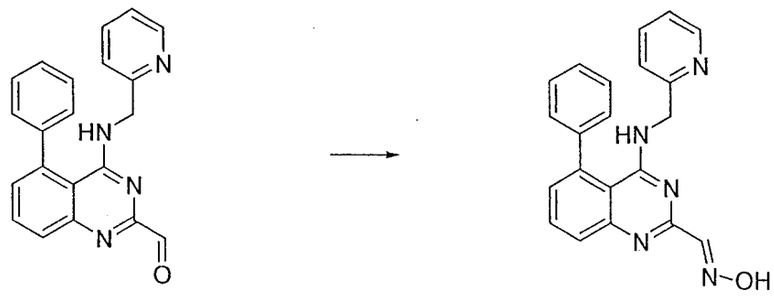
resultante se agitó a temperatura ambiente durante 4 horas. Después de este tiempo, la solución resultante se neutralizó con solución de $NaHCO_3$ saturada. El éter se evaporó y el residuo de la capa acuosa se extrajo en acetato de etilo. Los extractos orgánicos se secaron y se evaporaron. El residuo resultante se purificó mediante cromatografía en columna en gel de sílice (2 % de metanol en diclorometano) dando el Ejemplo 219 (56 mg, rendimiento del 62 %). RMN ^1H (400 MHz, DMSO-d_6) δ: 8,24 (a s, 1H); 7,80-7,63 (m, 3H); 7,54-7,44 (m, 5H); 7,24-7,20 (m, 3H); 6,56 (a s, 1H); 4,57 (s, 2H), 4,56 (d, 2H, J = 6 Hz); 3,77 (d, 4H, J = 6 Hz); 1,23 (s, 3H). CLEM Procedimiento W: tiempo de retención 1,77 min, [M+1] = 401; HPLC Procedimiento A1: pureza 95,14 %, tiempo de retención = 9,78 min.

EJEMPLO 220

3-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)isoxazol-5-carboxamida

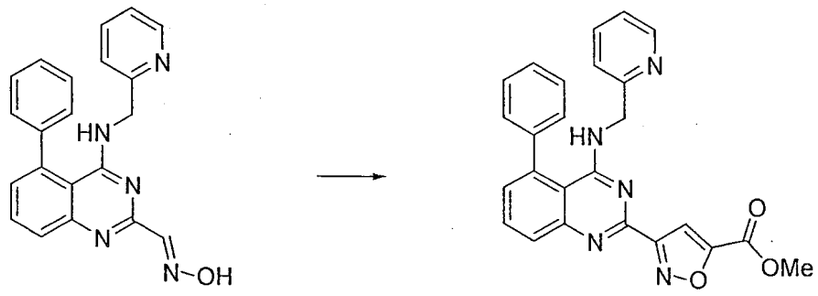


Etapa 1. Preparación de (E)-5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-carbaldehído



Una solución de 5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-carbaldehído (del ejemplo 212, 0,62 g, 1,8 mmol), clorhidrato de hidroxilamina (0,19 g, 2,8 mmol) y acetato sódico (0,30 g, 3,7 mmol) en agua (10 ml) se calentó a 100ºC durante 30 minutos. Después de este tiempo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente y después se extrajo con DCM (2 x 50 ml). Las porciones orgánicas combinadas se concentraron a presión reducida y el residuo resultante se purificó mediante cromatografía en gel de sílice (0,8% de MeOH en DCM) proporcionando (E)-5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-carbaldehído (0,4 g, rendimiento del 60 %) en forma de un sólido amarillo. CLEM Procedimiento W: tiempo de retención 1,703 min [M+1] = 356,2.

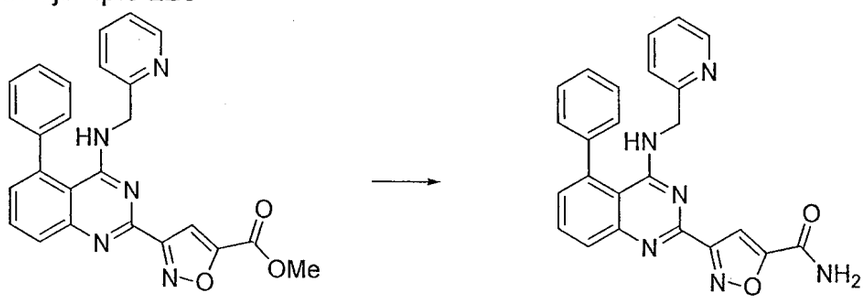
Etapa 2. Preparación de 3-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)isoxazol-5-carboxilato de metilo



000983

A una solución de oxima de (E)-5-fenil-4-(piridin-2-ilmetilamino)quinazolina-2-carbaldehído (0,32 g, 0,90 mmol) y metilpropriolato (0,227 g, 2,70 mmol) en acetonitrilo se añadió CrO_2 (Magtrieve) (0,75 g, 9,0 mmol). La mezcla de reacción se calentó a 80ºC durante 2 horas. Después de este tiempo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente. Una vez a la temperatura prescrita, la mezcla de reacción se diluyó con acetato de etilo y se filtró a través de celite. El filtrado se evaporó a presión reducida y el residuo resultante se purificó mediante cromatografía en gel de sílice (1,5% de MeOH en DCM) proporcionando 3-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)isoxazol-5-carboxilato de metilo (120 mg, rendimiento del 30%) en forma de un sólido blancuzco. CLEM Procedimiento W: tiempo de retención 2,185 min [M+1] = 438,2.

Etapa 3. Ejemplo 220

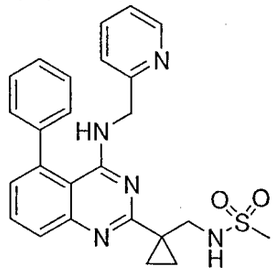


Una solución de 3-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)isoxazol-5-carboxilato (90 mg, 0,199 mmol) en NH_3 (2,0 M en MeOH, 5 ml) se calentó a 60ºC en un vaso sellado durante 8 horas. Después de este tiempo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiental y el

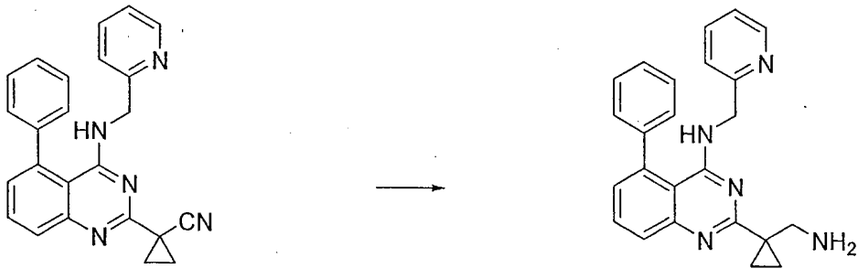
disolvente se evaporó a presión reducida. El residuo resultante se purificó mediante HPLC preparativa (Procedimiento S) proporcionando el Ejemplo 220 (35 mg, rendimiento del 42%). RMN ^{1}H (400 MHz, DMSO-d_6) δ: 8,45 (s, 1H); 8,21 (s, 1H); 8,05 (s, 1H); 7,92-7,85 (m, 2H); 7,73 (dt, 1H, J = 1,2, 7, 6 Hz); 7,67 (s, 1H); 7,60-7,49 (m, 5H); 7,40-7,30 (m, 3H); 7,24 (t, 1H, J = 5,6Hz); 7,00 (t, 1H, J = 4 Hz); 4,69 (d, 2H, J = 4 Hz). CLEM Procedimiento W: tiempo de retención 1,74 min, [M+1] = 423,2. HPLC Procedimiento A1: pureza 99,3 %, tiempo de retención = 6,78 min.

EJEMPLO 221

N-((1-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)ciclopropil)metil)metanosulfonamida

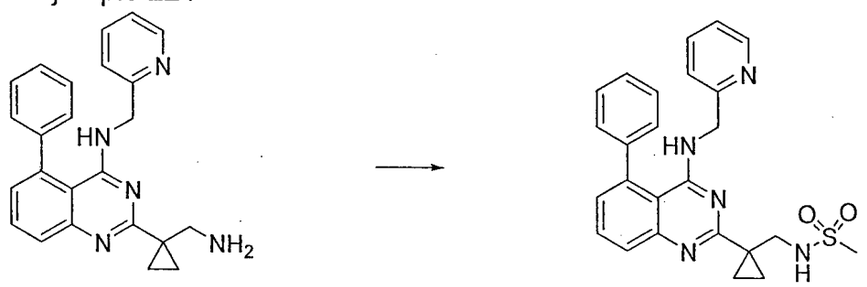


Etapa 1. Preparación de 2-(1-aminometil)ciclopropil)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina



A una solución de 1-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il) ciclopropanocarbonitrilo (Ejemplo 207, 0,6 g, 2 mmol) en metanol amoniaco 7M (10 ml) se añadió Ra-Ni (200 mg). La suspensión espesa resultante se agitó en atmósfera de nitrógeno durante 16 horas. Después de este tiempo, la mezcla de reacción se filtró y el filtrado se concentró a presión reducida dando 2-(1-(aminometil)ciclopropil)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (380 mg, rendimiento del 63 %), que se usó sin purificación adicional.

Etapa 2. Ejemplo 221

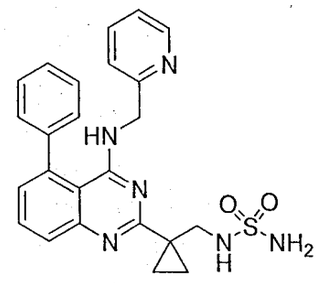


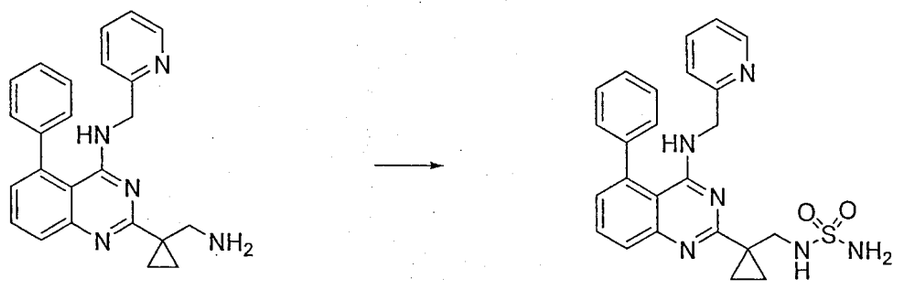
A una solución agitada de 2-(1-(aminometil)ciclopropil)-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (60 mg, 0,16 mmol) y TEA (0,05 ml, 0,43 mmol) en DCM (5 ml) se añadió cloruro de metanosulfonilo (0,015 ml, 0,18 mmol) gota a gota a 0ºC. Se dejó que la mezcla de reacción alcanzara la temperatura ambiente, temperatura a la que se agitó durante 2 horas. Después de este tiempo, la mezcla de reacción se inactivó con agua y después se extrajo con EtOAc. Los extractos orgánicos combinados se lavaron sucesivamente con agua y salmuera, se secaron y se filtraron. El filtrado se concentró a presión reducida dando un residuo. El residuo resultante se purificó mediante cromatografía en gel de sílice (15% de EtOAc, hexano), proporcionando el

Ejemplo 221 (25 mg, rendimiento del 36 %) en forma de un sólido blanco. RMN ^{1}H (400 MHz, DMSO-d_6) δ: 8,25 (d, 1H, J = 4,4 Hz); 7,80-7,68 (m, 3H); 7,60-7,43 (m, 5H); 7,27-7,15 (m, 3H); 6,95 (t, 1H, J = 6 Hz), 6,53 (s, 1H), 4,54 (d, 2H, J = 4 Hz), 3,54 (d, 2H, J = 6,4 Hz), 2,99 (s, 3H), 1,30 (d, 2H, J = 2,4 Hz, 1,01 (d, 2H, J = 2,4 Hz). CLEM Procedimiento V: tiempo de retención 1,77 min, [M+1] = 460,0; HPLC Procedimiento A1: pureza 99,1 %, tiempo de retención = 6,29 min.

EJEMPLO 222

N-((1-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)ciclopropil)metil)sulfamida



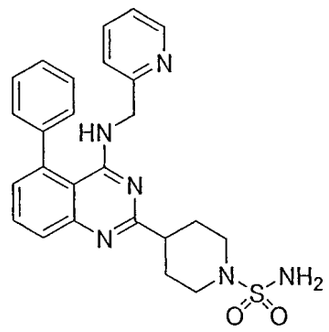


A una solución de clorosulfonilisocianato (0,03 ml, 0,2 mmol) en DCM (1 ml) se añadió t-BuOH (0,16 ml, 0,21 mmol) a 0ºC. La mezcla de reacción se agitó durante 10 minutos. Después de este tiempo, la mezcla de reacción se

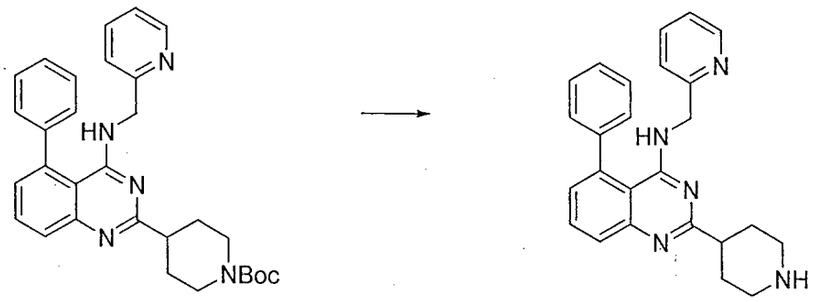
añadió a una mezcla de 2-(1-(aminometil)ciclopropil)-5-fenil-N-(piridin-2-ilmetil) quinazolin-4-amina (del ejemplo 221, 80 mg, 0,21 mmol) y TEA (0,043 ml, 0,42 mmol) en DCM a 0ºC. La mezcla de reacción resultante se agitó durante 3 horas adicionales a temperatura ambiente. Al finalizar este periodo, la mezcla de reacción se inactivó con agua (15 ml) y después se extrajo con DCM. Los extractos orgánicos combinados se lavaron sucesivamente con agua y salmuera, se secaron con Na_2SO_4, se filtraron y se concentraron a presión reducida dando un residuo. Se añadió TFA (2 ml) al residuo y la mezcla de reacción resultante se agitó durante 2 horas y después se concentró al vacío. El residuo resultante se diluyó con EtOAc (20 ml) y se lavó sucesivamente con $NaHCO_3$ saturado y salmuera, se secó sobre Na_2SO_4, se filtró y el disolvente se eliminó a presión reducida. El residuo resultante se purificó mediante cromatografía en gel de sílice (5 % de MeOH en DCM) dando el Ejemplo 222 (25 mg, rendimiento del 27 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ: 8,24 (dd, 1H, J = 1,2Hz, 7,2Hz); 7,67-7,80 (m, 3H); 7,58-7,43 (m, 5H); 7,28-7,16 (m, 3H); 6,63 (s, 2H), 6,53 (a s, 1H), 6,48-6,43 (m, 1H), 4,52(d, 2H, J = 4Hz), 3,45 (d, 2H, J = 7,6 Hz), 1,28 (d, 2H, J = 4 Hz), 1,02 (d, 2H, J = 4 Hz). CLEM Procedimiento W: tiempo de retención 1,93 min, [M+1] = 461,2; HPLC Procedimiento A1: pureza 96,5 %, tiempo de retención = 5,91 min.

EJEMPLO 223

4-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piperidin-1-sulfonamida



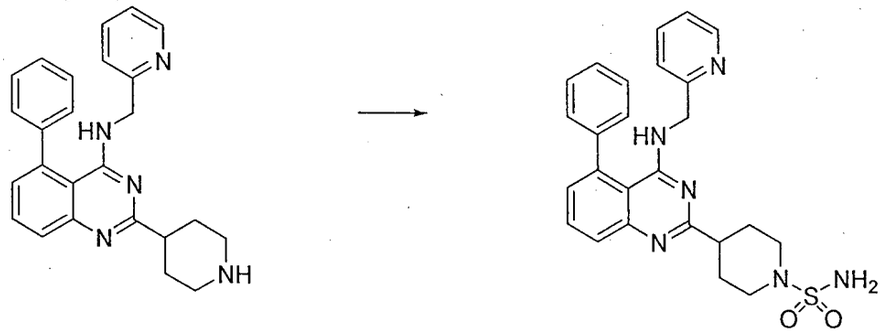
Etapa 1. Preparación de 5-fenil-2-(piperidin-4-il)-N-(piridin-2-ilmetil)quinazolin-4-amina



El compuesto 4-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)piperidin-1-carboxilato de terc-butilo (Ejemplo 211, 0,2 g 0,4 mmol) se disolvió en 10 ml de HCl (2M en éter). La mezcla de reacción se agitó a temperatura ambiente durante 16 horas. Después de este tiempo, el disolvente se eliminó a presión reducida. El residuo resultante se neutralizó con $NaHCO_3$ sat. y la fase acuosa se extrajo en DCM. . Los extractos orgánicos combinados se concentraron a presión reducida y el residuo resultante se purificó mediante recristalización con EtOAc dando 5-fenil-2-(piperidin-4-il)-N-(piridin-2-ilmetil)quinazolin-4-amina (0,13 g, rendimiento del 76 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,21 (d, 1H, J = 4,0 Hz), 7,77-7,66 (m, 3H), 7,58-7,40 (m, 5H), 7,30-7,15 (m, 3H), 6,57 (a s, 1H), 4,56 (d, 2H, J = 4,0 Hz), 3,05 (d, 2H, J = 12,0 Hz), 2,80-2,70 (m, 1H), 2,60 (t, 2H, J = 8,0 Hz), 1,95-1,80 (m, 2H), 1,80-1,65 (m, 2H), CLEM

Procedimiento W: tiempo de retención 1,43 min, [M+1] = 396,2; HPLC Procedimiento A1: pureza 96,4 %, tiempo de retención = 9,00 min.

Etapa 2. Ejemplo 223

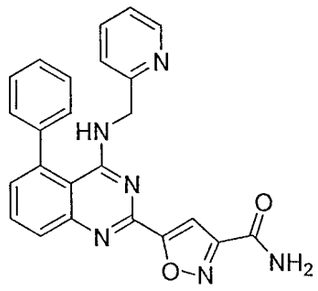


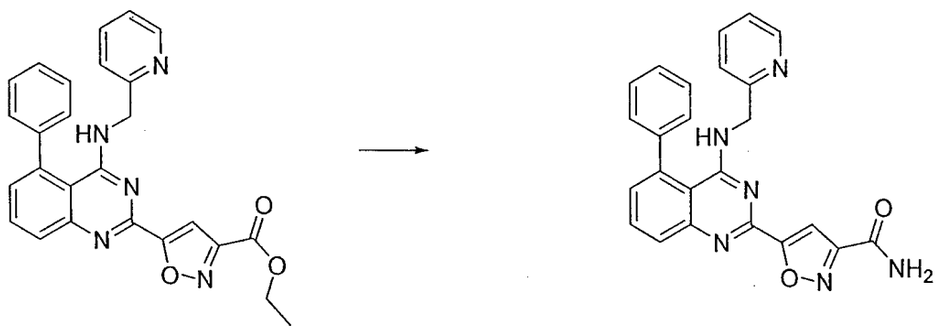
A una solución de clorosulfonilisocianato (0,035 ml, 0,25 mmol) en DCM (5 ml) se añadió t-BuOH (0,19 g, 0,25 mmol) a temperatura ambiente. La mezcla de reacción se agitó durante 10 minutos y después se añadió TEA (0,038 g, 0,37 mmol), seguido por 5-fenil-2-(piperidin-4-il)-N-(piridin-2-ilmetil)quinazolin-4-amina (0,1 g, 0,3 mmol) en DCM. La mezcla de reacción resultante se agitó a temperatura ambiente durante 3 horas adicionales. Después de este tiempo, la mezcla de reacción se diluyó con agua y después se extrajo en EtOAc. Los extractos orgánicos combinados se secaron y se concentraron a presión reducida, dando un residuo. El residuo se trató con HCl etéreo (4 ml, solución 2M). La solución resultante se concentró a presión reducida y el residuo resultante se purificó mediante recristalización usando EtOAc dando el ejemplo 223 (0,038 g, rendimiento del 32%). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,20 (s, 1H), 7,80-7,66 (m, 3H), 7,58-7,43 (m, 5H), 7,27 (d, 1H, J = 8,0 Hz), 7,24-7,18 (m, 2H), 6,73 (a s, 2H),6,65 (t, 1H, J = 4,0 Hz), 4,58 (d, 1H, J = 8,0 Hz), 3,55 (d, 2H, J = 12,0 Hz), 2,81-2,64 (m, 3H), 2,10-

2,04 (m, 2H), 2,00-1,86 (m, 2H). CLEM Procedimiento V: tiempo de retención 1,62 min, [M+1] = 475; HPLC Procedimiento A1: pureza 98,7 %, tiempo de retención = 6,26 min.

EJEMPLO 224

5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)isoxazol-3-carboxamida





Una solución de 5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)isoxazol-3-carboxilato de etilo (del ejemplo 209, 0,075 g, 0,17 mmol) en NH_3 (2,0 M en MeOH, 5 ml) se calentó a 60ºC en un vaso sellado durante 16 horas. Después de este tiempo, la mezcla de reacción se dejó enfriar hasta la temperatura ambiente. Una vez a la temperatura prescrita, el sólido formado se filtró y se lavó con metanol enfriado con hielo proporcionando el Ejemplo 224

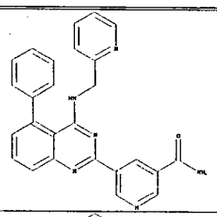
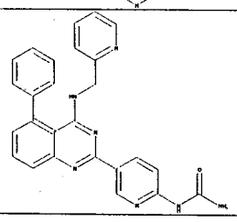
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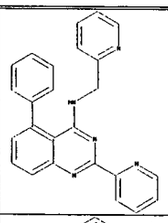
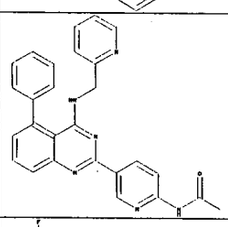
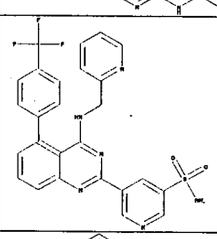
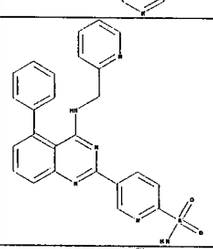
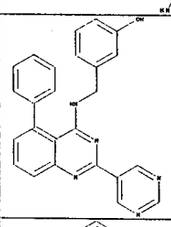
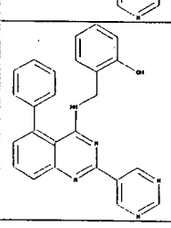
(31 mg, rendimiento del 44%). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,29 (s, 1H), 8,21 (d, 1H, J = 2 Hz), 7,87-7,95 (m, 3H), 7,73 (dt, 1H, J = 1,6, 8 Hz), 7,45-7,64 (m, 5H), 7,37 (dt, 2H, J = 1,6, 6,8 Hz, 2H), 7,25 (dd, 1H, J = 6,0, 7,2 Hz), 4,70 (d, 2H, J = 4 Hz). CLEM Procedimiento W: tiempo de retención 1,817 min, [M+1] = 423,2; HPLC Procedimiento A1: pureza 99,3 %, tiempo de retención = 7,31 min.

EJEMPLOS 225 A 322-{}-

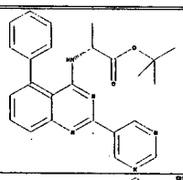
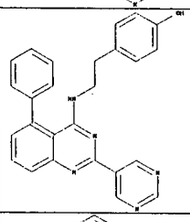
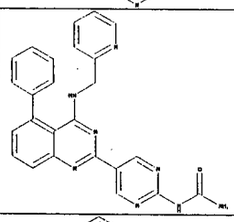
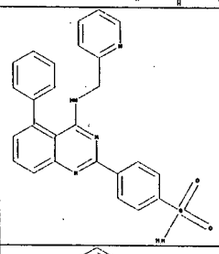
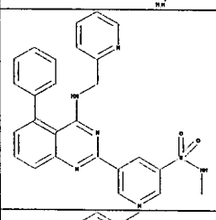
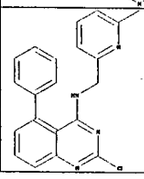
Los Ejemplos 225 a 322 se sintetizaron mediante procedimientos similares a los descritos en lo que antecede. Los datos de HPLC/EM para cada compuesto se recogieron usando los procedimientos E-Z1 y la masa molecular se determinó mediante EM (ES) mediante la fórmula m/z. Tanto el tiempo de retención como los datos de EM para los Ejemplos 225 a 322 se indican en la Tabla 1c, en la que PM= peso molecular.

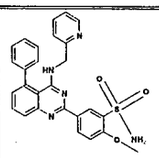
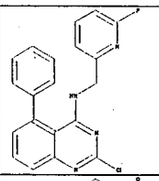
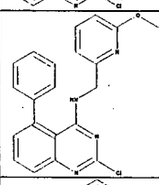
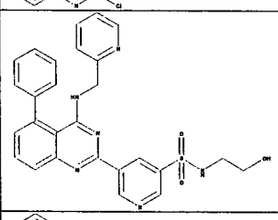
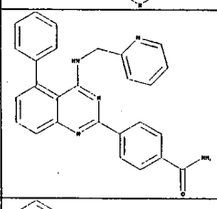
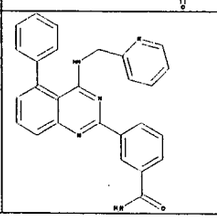
TABLA 1c

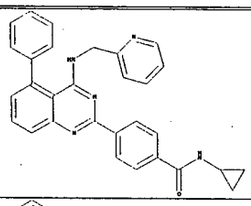
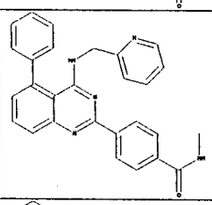
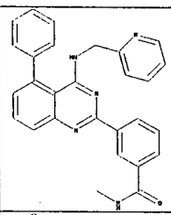
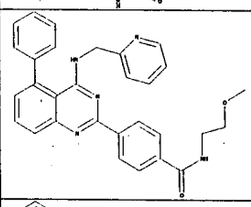
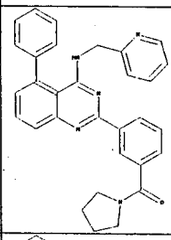
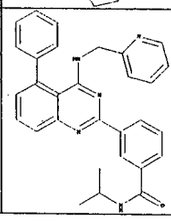
Ejemplo	**Estructura**	**PM**	Datos de CLEM	Procedimiento de CLEM
225		432,477	[M+1] 433,0 Tr1,86 min	E
226		447,491	[M+1] 448,0 Tr1,50 min	O

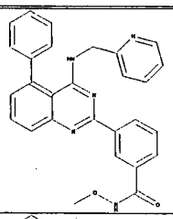
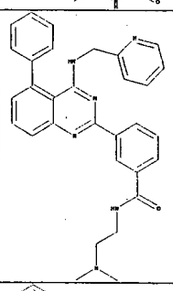
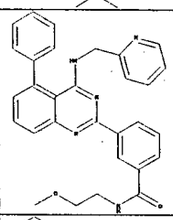
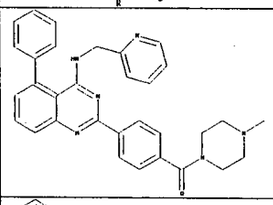
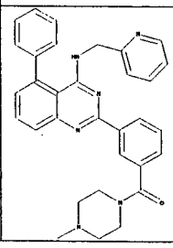
Ejemplo	**Estructura**	**PM**	Datos de CLEM	Procedimiento de CLEM
227		389,452	[M+1] 390,0 Tr1,58 min	O
228		446,503	[M+1] 447,0 Tr1,49 min	O
229		536,528	[M+1] 537,0 Tr1,73 min	O
230		468,53	[M+1] 469,0 Tr1,41 min	O
231		405,451	[M+1] 406,2 Tr2,50 min	Z1
232		405,451	[M+1] 406,2 Tr2,58 min	Z1

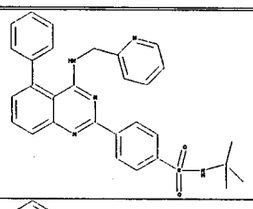
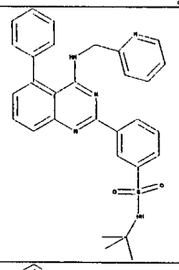
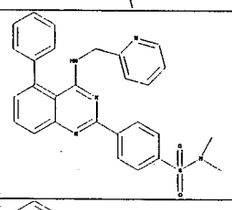
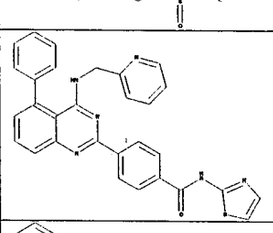
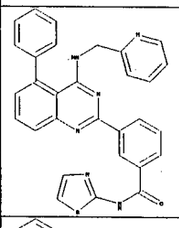
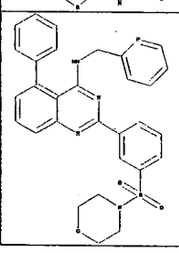
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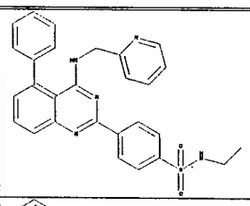
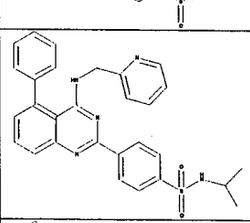
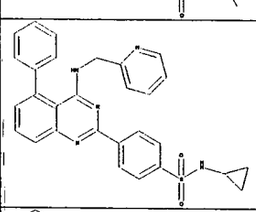
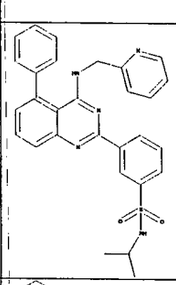
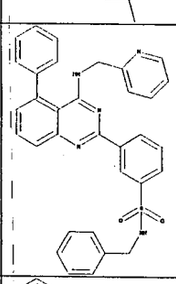
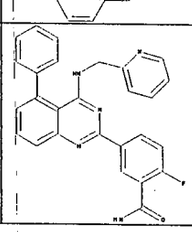
Ejemplo	**Estructura**	**PM**	Datos de CLEM	Procedimiento de CLEM
233		427,498	[M+1] 428,2 Tr3,12 min	Z1
234		419,478	[M+1] 420,2 Tr2,56 min	Z1
235		448,479	[M+1] 449,2 Tr1,89 min	Y
236		467,542	[M+1] 468,2 Tr1,98 min	Y
237		482,557	[M+1] 483,2 Tr1,99 min	Y
238		360,839	[M+1] 361,20 Tr1,55 min	T

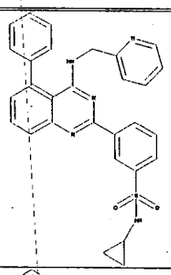
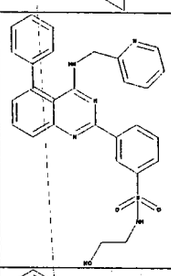
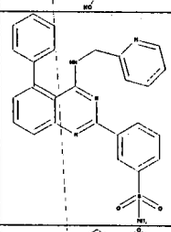
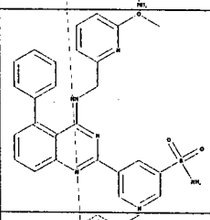
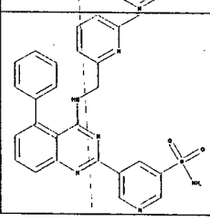
Ejemplo	**Estructura**	**PM**	Datos de CLEM	Procedimiento de CLEM
239		497,568	[M+1] 498,2 Tr1,48 min	T
240		364,803	[M+1] 365,2 Tr2,05 min	T
241		376,839	[M+1] 377,2 Tr2,14 min	T
242		512,583	[M+1] 513,2 Tr1,80 min	Y
243		431,489	[M+1] 432,2 Tr2,40 min	Z1
244		431,489	[M+1] 432,2 Tr2,40 min	Z1

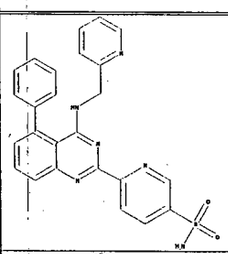
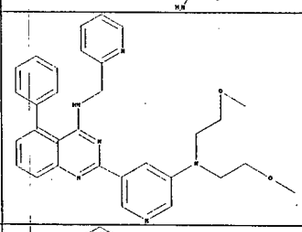
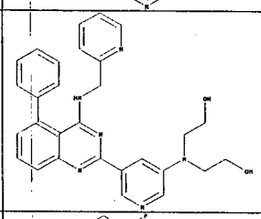
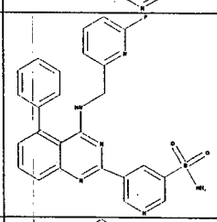
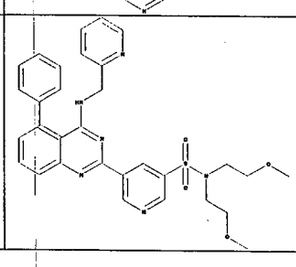
Ejemplo	**Estructura**	**PM**	Datos de CLEM	Procedimiento de CLEM
245		471,552	[M+1] 472,2 Tr2,68 min	Z1
246		445,515	[M+1] 446,2 Tr2,50 min	Z1
247		445,515	[M+1] 446,2 Tr2,53 min	Z1
248		489,568	[M+1] 490,2 Tr2,59 min	Z1
249		485,579	[M+1] 486,2 Tr2,84 min	Z1
250		473,568	[M+1] 474,2 Tr2,87 min	Z1

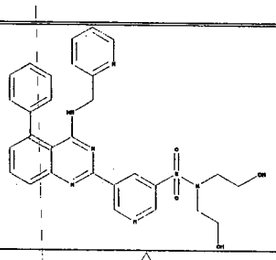
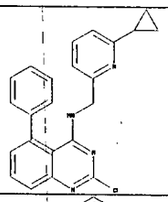
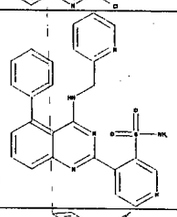
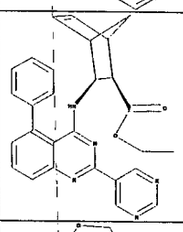
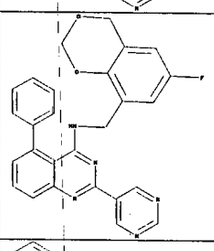
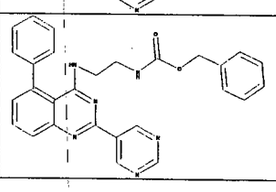
Ejemplo	**Estructura**	**PM**	Datos de CLEM	Procedimiento de CLEM
251		461,515	[M+1] 462,2 Tr2,52 min	Z1
252		502,609	[M+1] 503,2 Tr2,57 min	Z1
253		489,568	[M+1] 490,2 Tr2,63 min	Z1
254		514,62	[M+1] 515,2 Tr2,58 min	Z1
255		514,62	[M+1] 515,2 Tr2,58 min	Z1

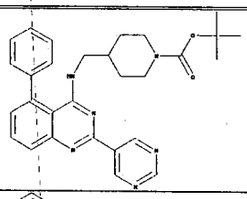
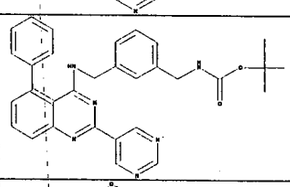
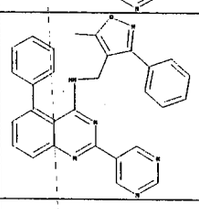
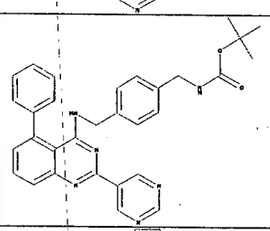
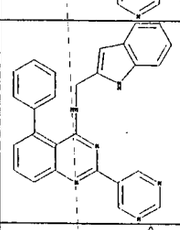
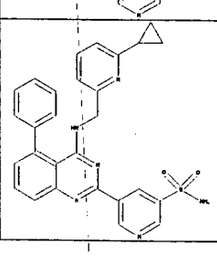
Ejemplo	**Estructura**	**PM**	Datos de CLEM	Procedimiento de CLEM
256		523,649	[M+1] 524,2 Tr3,24 min	Z1
257		523,649	[M+1] 524,2 Tr3,23 min	Z1
258		495,595	[M+1] 496,2 Tr3,13 min	Z1
259		514,6	[M+1] 515,2 Tr2,99 min	Z1
260		514,6	[M+1] 515,2 Tr3,04 min	Z1
261		537,632	[M+1] 538,2 Tr3,05 min	Z1

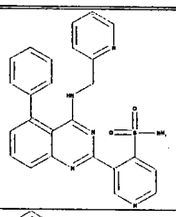
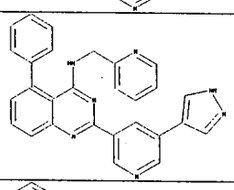
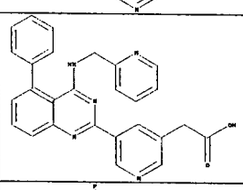
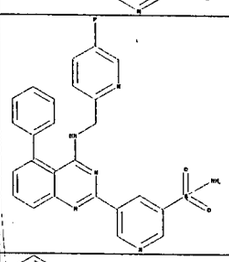
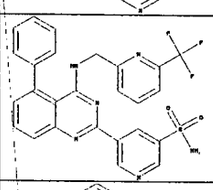
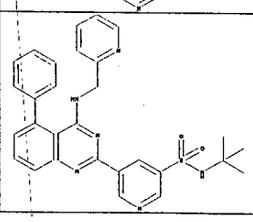
Ejemplo	**Estructura**	**PM**	Datos de CLEM	Procedimiento de CLEM
262		495,595	[M+1] 496,2 Tr2,96 min	Z1
263		509,622	[M+1] 510,2 Tr3,10 min	Z1
264		507,606	[M+1] 508,2 Tr3,01 min	Z1
265		509,622	[M+1] 510,2 Tr3,09 min	Z1
266		557,665	[M+1] 558,2 Tr3,23 min	Z1
267		449,479	[M+1] 450,2 Tr2,54 min	Z1

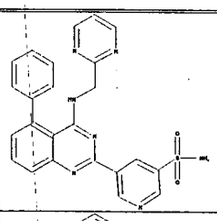
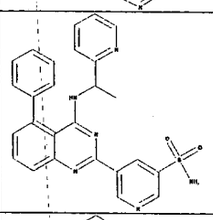
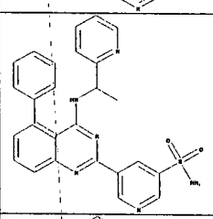
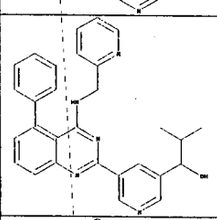
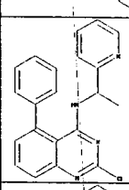
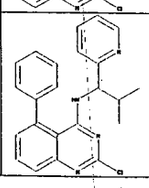
Ejemplo	**Estructura**	**PM**	Datos de CLEM	Procedimiento de CLEM
268		507,606	[M+1] 508,2 Tr2,99 min	Z1
269		511,595	[M+1] 512,2 Tr2,50 min	Z1
270		467,542	[M+1] 468,2 Tr2,53 min	Z1
271		498,556	[M+1] 499,2 Tr2,03 min	W
272		482,557	[M+1] 483,2 Tr1,91 min	W

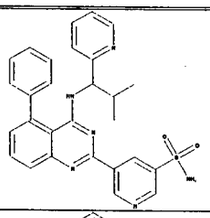
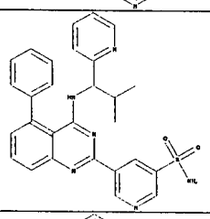
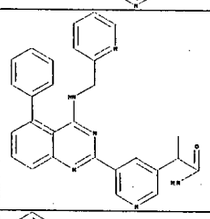
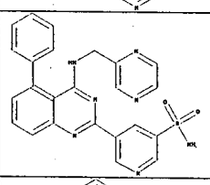
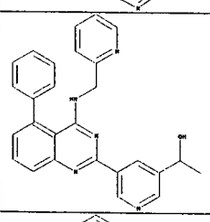
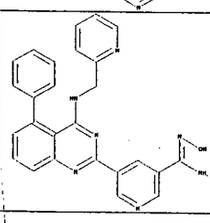
Ejemplo	**Estructura**	**PM**	Datos de CLEM	Procedimiento de CLEM
273		468,53	[M+1] 469,2 Tr1,52 min	T
274		520,625	[M+1] 521,2 Tr1,76 min	T
275		492,572	[M+1] 493,4 Tr1,73 min	Y
276		486,521	[M+1] 487,2 Tr1,95 min	W
277		584,689	[M+1] 585,2 Tr1,83 min	T

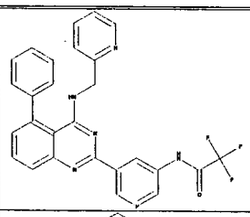
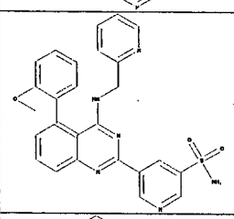
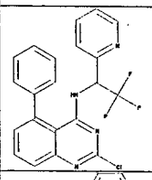
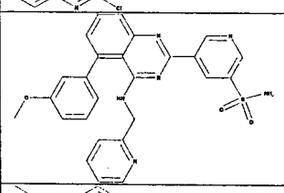
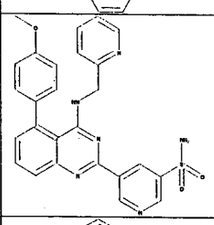
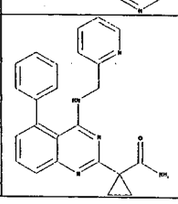
Ejemplo	**Estructura**	**PM**	Datos de CLEM	Procedimiento de CLEM
278		556,635	[M+1] 557,2 Tr1,56 min	T
279		386,877	[M+1] 387,2 Tr2,17 min	Y
280		468,53	[M+1] 469,2 Tr1,84 min	Y
281		463,53	[M+1] 464,2 Tr3,16 min	Z1
282		465,478	[M+1] 466,2 Tr3,00 min	Z1
283		476,529	[M+1] 477,2 Tr2,74 min	Z1

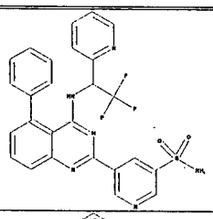
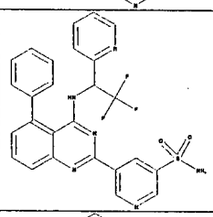
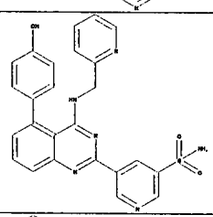
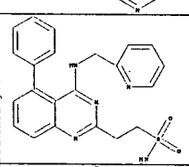
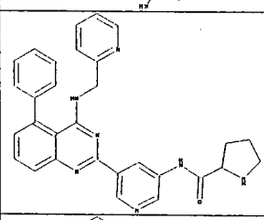
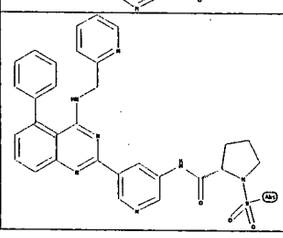
Ejemplo	**Estructura**	**PM**	Datos de CLEM	Procedimiento de CLEM
284		496,603	[M+1] 497,2 Tr3,34 min	Z1
285		518,609	[M+1] 519,2 Tr3,17 min	Z1
286		470,525	[M+1] 471,2 Tr2,97 min	Z1
287		518,609	[M+1] 519,2 Tr3,16 min	Z1
288		428,488	[M+1] 429,2 Tr3,01 min	Z1
289		508,594	[M+1] 509,2 Tr1,58 min	T

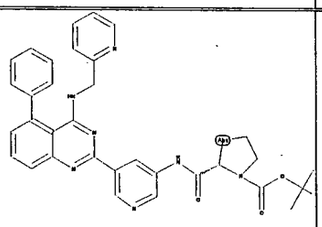
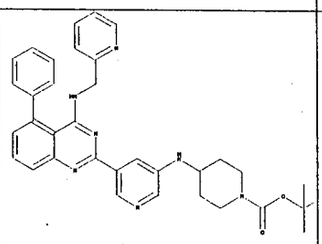
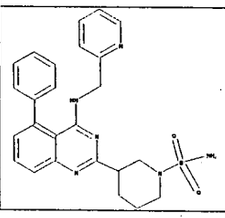
Ejemplo	**Estructura**	**PM**	Datos de CLEM	Procedimiento de CLEM
290		468,53	[M+1] 469,2 Tr1,42 min	T
291		455,513	[M+1] 456,2 Tr1,86 min	Y
292		447,488	[M+1] 448,2 Tr1,36 min	W
293		486,521	[M-1] 485,0 Tr1,93 min	Y
294		536,528	[M+1] 537,0 Tr1,96 min	T
295		524,637	[M-1] 523,2 Tr2,10 min	Y

Ejemplo	**Estructura**	**PM**	Datos de CLEM	Procedimiento de CLEM
296		469,518	[M+1] 470,2 Tr1,64 min	T
297		482,557	[M+1] 483,2 Tr1,66 min	T
298		482,557	[M+1] 483,2 Tr1,65 min	T
299		461,558	[M+1] 462,2 Tr1,78 min	T
300		360,839	[M+1] 361,0 Tr1,87 min	T
301		388,893	[M+1] 389,2 Tr1,98 min	T

Ejemplo	**Estructura**	**PM**	Datos de CLEM	Procedimiento de CLEM
302		510,61	[M+1] 511,2 Tr1,79 min	T
303		510,61	[M+1] 511,2 Tr1,79 min	T
304		460,53	[M+1] 461,0 Tr1,78 min	Y
305		469,518	[M+1] 470,0 Tr1,72 min	W
306		433,504	[M+1] 434,2 Tr1,60 min	V
307		447,491	[M+1] 447,9 Tr1,79 min	Y

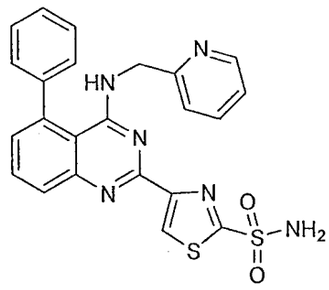
Ejemplo	**Estructura**	**PM**	Datos de CLEM	Procedimiento de CLEM
308		500,475	[M-1] 499,0 Tr1,75 min	V
309		498,556	[M+1] 499,2 Tr1,83 min	W
310		414,811	[M+1] 415,0 Tr2,16 min	T
311		498,556	[M+1] 499,2 Tr1,87 min	W
312		498,556	[M+1] 499,2 Tr1,64 min	V
313		395,456	[M+1] 396,2 Tr1,43 min	T

Ejemplo	**Estructura**	**PM**	Datos de CLEM	Procedimiento de CLEM
314		536,528	[M+1] 537,2 Tr2,05 min	T
315		536,528	[M+1] 537,2 Tr2,05 min	T
316		484,53	[M+1] 485,2 Tr1,69 min	Y
317		419,499	[M-1] 418,0 Tr1,73 min	Y
318		501,582	[M+1] 502,2 Tr1,58 min	V
319		579,672	[M+1] 580,2 Tr1,87 min	W

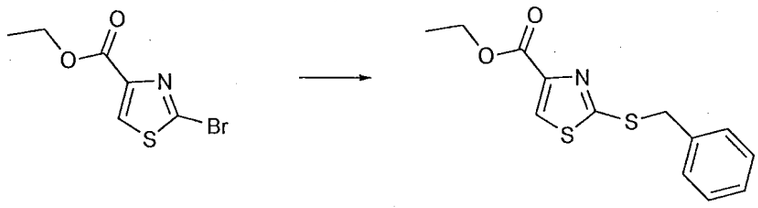
Ejemplo	**Estructura**	**PM**	Datos de CLEM	Procedimiento de CLEM
320		601,697	[M-1] 600,2 Tr2,16 min	W
321		587,714	[M+1] 588,2 Tr1,865 min	V
322		474,578	[M+1] 475,2 Tr1,84 min	W

EJEMPLO 323

4-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)tiazol-2-sulfonamida

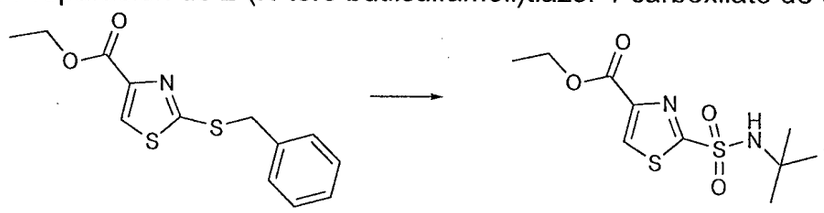


Etapa 1. Preparación de 2-(benciltio)tiazol-4-carboxilato de etilo



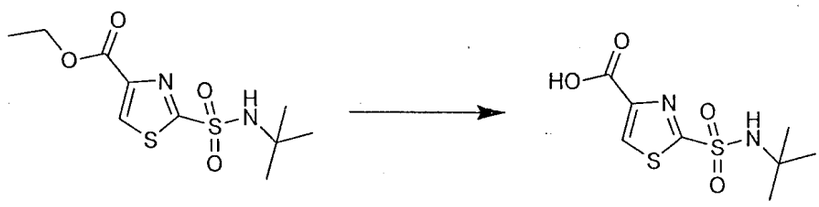
A una solución de 2-bromotiazol-4-carboxilato de etilo (2,0 g, 8,40 mmol) en DMF (15 ml) se añadió K_2CO_3 (1,16 g, 8,40 mmol), seguido por bencilmercaptano (1,07 g, 8,40 mmol) en DMF (5 ml) durante 20 minutos. Tras finalizar la adición, la mezcla de reacción se agitó a temperatura ambiente durante 16 horas. Después de este tiempo, la mezcla de reacción se diluyó con agua y se extrajo en EtOAc. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El concentrado resultante se purificó mediante cromatografía en gel de sílice (10 % de EtOAc en hexano) proporcionando 2-(benciltio)tiazol-4-carboxilato de etilo (2,0 g, rendimiento del 87 %). RMN ^{1}H (400 MHz, DMSO-d_6) δ (ppm): 8,42 (s, 1H); 7,47-45 (m, 2H); 7,36-7,28 (m, 3H); 4,52 (s, 2H); 4,31(c, 2H, J = 7,2Hz); 1,31 (t, 3H, J = 7,2Hz).

Etapa 2. Preparación de 2-(N-terc-butilsulfamoil)tiazol-4-carboxilato de etilo



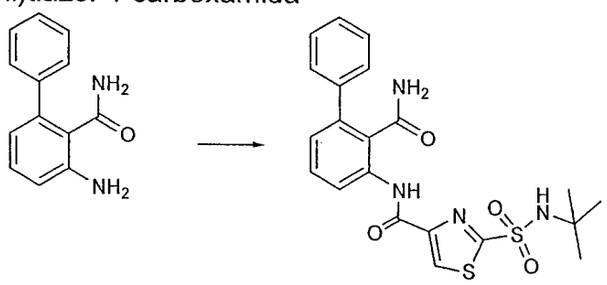
Una solución de 2-(benciltio)tiazol-4-carboxilato de etilo (2,0 g, 7,10 mmol) en CCl_4/H_2O (100/10 ml) se enfrió hasta 0-5ºC. Se introdujeron burbujas de gas cloro a través de la solución durante 30 minutos. Después de este tiempo, el exceso de gas cloro se evaporó aclarando con una corriente de nitrógeno. La mezcla de reacción se diluyó después con diclorometano y se lavó con salmuera. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, se filtraron y se concentraron dando el cloruro de sulfonilo bruto. El cloruro de sulfonilo bruto se disolvió en THF (50 ml), seguido por la adición de terc-butilamina (10 ml) en tubo sellado. El contenido del tubo se calentó hasta 60ºC durante 16 horas. Al finalizar este periodo se evaporaron los volátiles. El residuo resultante se lavó con agua y se extrajo con EtOAc. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, se filtraron y se concentraron proporcionando 2-(N-terc-butilsulfamoil)tiazol-4-carboxilato de etilo (1,8 g, rendimiento del 90%) en forma de un sólido blancuzco. RMN ^1H (400 MHz, DMSO-d_6) δ (ppm): 8,78 (s, 1H); 8,0 (a s, 1H); 4,34 (c, 2H, J = 7,2 Hz); 1,31 (t, 3H, J = 7,2 Hz); 1,18 (s, 9H).

Etapa 3. Preparación de 2-(N-terc-butilsulfamoil)tiazol-4-carboxilato de etilo



A una solución de 2-(N-terc-butilsulfamoil)tiazol-4-carboxilato de etilo (1,8 g, 6,1 mmol) en 50 ml de THF-EtOH (1:1) se añadió LiOH (0,07 g, 18,3 mmol). La mezcla resultante se agitó durante 4 horas. Después de este tiempo, la mezcla de reacción se neutralizó con HCl (1,0M ac.), se diluyó con agua y después se extrajo con EtOAc. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, se filtraron y se concentraron proporcionando 2-(N-terc-butilsulfamoil)tiazol-4-carboxilato de etilo (1,6g, rendimiento del 99%) en forma de un sólido blanco. CLEM Procedimiento V: tiempo de retención 0,93 min [M+1] = 263,0.

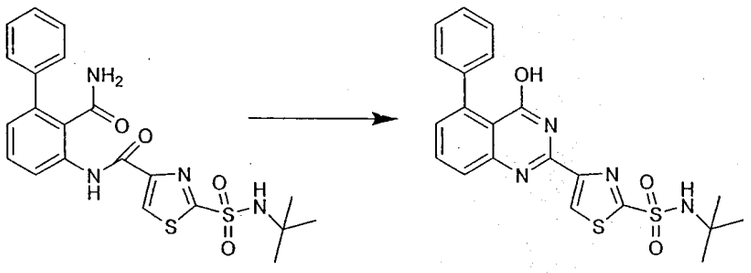
Etapa 4. Preparación de 2-(N-terc-butilsulfamoil)-N-(2-carbamoilbifenil-3-il)tiazol-4-carboxamida



A una solución de ácido 2-(N-terc-butilsulfamoil)tiazol-4-carboxílico (0,56 g, 2,1 mmol) en DCM (50 ml) se añadió HTU (1,41 g, 2,8 mmol) y DIPEA (1,04 ml, 5,6 mmol). La mezcla de reacción se agitó a temperatura ambiente durante 1 hora y después se añadió 3-aminobifenil-2-carboxamida (del ejemplo 218, 0,3 g, 1,4 mmol). La solución resultante se agitó durante 16 horas adicionales.

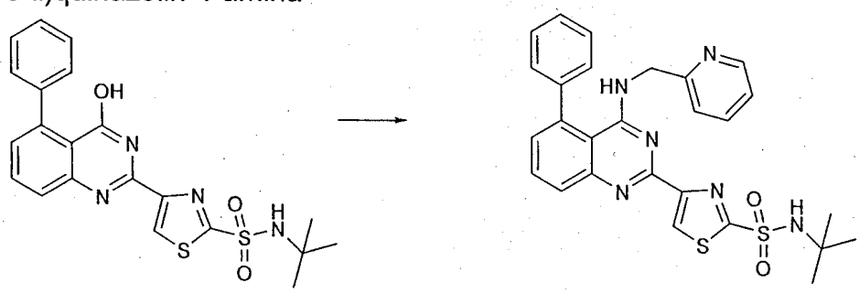
Después de este tiempo, la mezcla de reacción se lavó con agua, se secó, se filtró y se concentró a presión reducida dando un residuo. El residuo se purificó mediante cromatografía en gel de sílice (30% de EtOAc en hexano) proporcionando 2-(N-terc-butilsulfamoil)-N-(2-carbamoilbifenil-3-il)tiazol-4-carboxamida (0,11g, rendimiento del 17%) en forma de sólido blanco. CLEM Procedimiento V: tiempo de retención 1,85 min [M+1] = 459,2.

Etapa 5.Preparación de (N-terc-butil-4-(4-hidroxi-5-fenilquinazolin-2-il)tiazol-2-sulfonamida



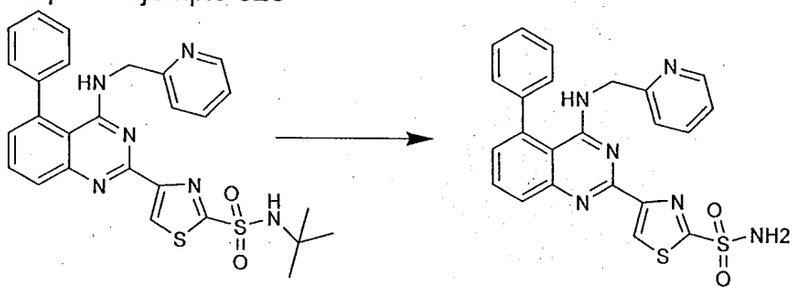
A una solución de 2-(N-terc-butilsulfamoil)-N-(2-carbamoilbifenil-3-il)tiazol-4-carboxamida (0,11 g, 0,24 mmol) en metanol (10 ml) se añadió NaOMe (0,25 ml, 25% en MeOH, 1,2 mmol). La mezcla resultante se agitó a temperatura ambiente durante 16 horas. Después de este tiempo, la mezcla de reacción se concentró, se diluyó con acetato de etilo y se lavó con agua. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El residuo resultante se purificó mediante cromatografía en gel de sílice (40 % de EtOAc en hexano) proporcionando (N-terc-butil-4-(4-hidroxi-5-fenilquinazolin-2-il)tiazol-2-sulfonamida (0,10 g, rendimiento del 100 %) en forma de sólido blanco. CLEM Procedimiento V: tiempo de retención 2,01 min [M+1] = 441,2.

Etapa 6. Preparación de 5-fenil-N-(piridin-2-ilmetil)-2-(2,2,5-trimetil)-1,3-dioxan-5-il)quinazolin-4-amina



A una solución de 5-fenil-2-(2,2,5-trimetil-1,3-dioxan-5-il)quinazolin-4(3H)-ona (0,22 g, 0,62 mmol) en MeCN (10 ml) a temperatura ambiente se añadió DBU (0,24 g, 1,57 mmol) y reactivo BOP (0,36 g, 0,81 mmol). Tras finalizar la adición, la mezcla de reacción se agitó durante 30 minutos. Se añadió aminometilpiridina (0,11, 1,13 mmol) y la mezcla resultante se agitó durante 16 horas adicionales. Después de este tiempo, la mezcla de reacción se concentró y se purificó mediante cromatografía en columna en gel de sílice (2% de MeH en DCM) proporcionando 5-fenil-N-(piridin-2-ilmetil)-2-(2,2,5-trimetil-1,3-dioxan-5-il)quinazolin-4-amina (0,18 g, rendimiento del 68 %) en forma de un sólido blanco. CLEM Procedimiento V: tiempo de retención 2,21 min [M+1] = 531,2.

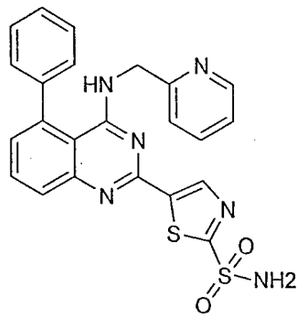
Etapa 7. Ejemplo 323



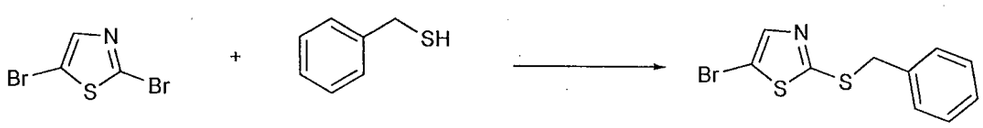
Una solución de N-terc-butil-4-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)tiazol-2-sulfonamida (0,05 g 0,10 mmol) en TFA (10 ml) se calentó a 50ºC durante 8 horas. Después de este tiempo, el TFA se evaporó a presión reducida dando un residuo. El residuo se basificó mediante la adición de 10% de bicarbonato sódico y después se extrajo en DCM. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El residuo resultante se purificó mediante recristalización usando DCM/hexano proporcionando el Ejemplo 323 (30 mg, rendimiento de l78 %) en forma de un sólido Amarillo marronáceo. RMN ^{1}H (400 MHz, DMSO-d_6) δ: 8,80 (s, 1H); 8,25 (s, 1H); 8,19 (a s, 1H); 7,90-7,80 (m, 2h); 7,65 (dt, 1H, J = 1,6, 6,8 Hz); 7,60-7,48 (m, 5H); 7,32-7,20 (m, 3H); 6,78 (t, 1H, J = 4 Hz); 4,71 (d, 2H, J = 4 Hz), CLEM Procedimiento R: tiempo de retención 1,65 min, [M+1] = 472,8; HPLC Procedimiento A1: pureza 95,8 %, tiempo de retención = 12,5 min.

EJEMPLO 324

5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)tiazol-2-sulfonamida

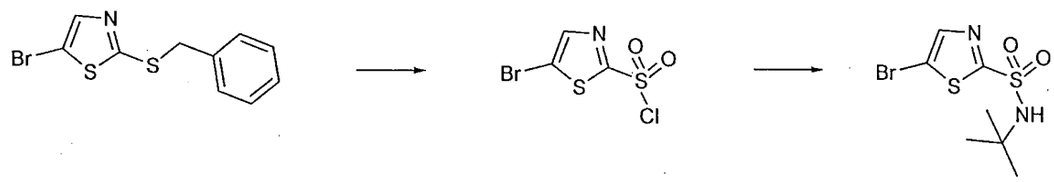


Etapa 1. Preparación de 2-(benciltio)-5-bromotiazol



A una solución de 2,5-dibromotiazol (2,0 g, 8,23 mmol) en DMF (15 ml) se añadió K_2CO_3 (1,16 g, 8,40 mmol) seguido por bencilmercaptano (1,07 g, 8,40 mmol) en DMF (10 ml) durante un periodo de 20 minutos. La mezcla de reacción se agitó a temperatura ambiente durante la noche. Después de este tiempo, la mezcla de reacción se diluyó con agua y se extrajo en EtOAc. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, se filtraron y se concentraron a presión reducida. El producto bruto resultante se purificó mediante cromatografía en gel de sílice (0,2 % de EtOAc en hexano) dando 2-(benciltio)-5-bromotiazol (2,3 g, rendimiento del 97,5 %) en forma de un sólido marrón. RMN ^{1}H (400 MHz, DMSO-d_6) δ: 7,56 (s, 1H); 7,25-7,36 (m, 5H); 4,39 (s, 2H). ^{1}H CLEM Procedimiento V: tiempo de retención 2,319 min [M+1] = 286.

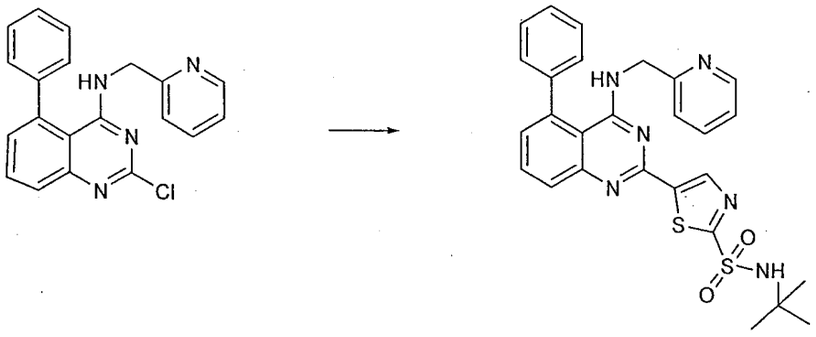
Etapa 2. Preparación de 5-bromo-N-terc-butiltiazol-2-sulfonamida



Una solución de 2-(benciltio)-5-bromotiazol (2,3 g, 8,00 mmol) se disolvió en CCl_4 / H_2O (100/10 ml) y después se enfrió hasta 0-5ºC. Se introdujo gas cloro mediante burbujas a través de la mezcla de reacción durante 30 minutos. Después de este tiempo, el exceso de gas cloro se

evaporó aclarando la mezcla de reacción con una corriente de nitrógeno. La mezcla de reacción se diluyó con diclorometano y se lavó con salmuera. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, se filtraron y se concentraron proporcionando el cloruro de sulfonilo bruto. El cloruro de sulfonilo bruto se disolvió en THF (50 ml), y después terc-butilamina (10 ml) en tubo sellado. El contenido del tubo se calentó hasta 60ºC durante 16 horas. Después de este tiempo se evaporaron los volátiles y se lavaron con agua y se extrajeron en EtOAc. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, se filtraron y se concentraron. El residuo resultante se purificó mediante cromatografía en gel de sílice (10% de EtOAc/hexano) proporcionando 5-bromo-N-terc-butiltiazol-2-sulfonamida (1,0 g, rendimiento del 41,5 %) en forma de un sólido blanco. RMN ^{1}H (400 MHz, DMSO-d_6) δ: 8,41 (s, 1H); 8,17 (s, 1H); 1,25 (s, 9H). CLEM Procedimiento V: tiempo de retención 1,861 min [M-1] = 297

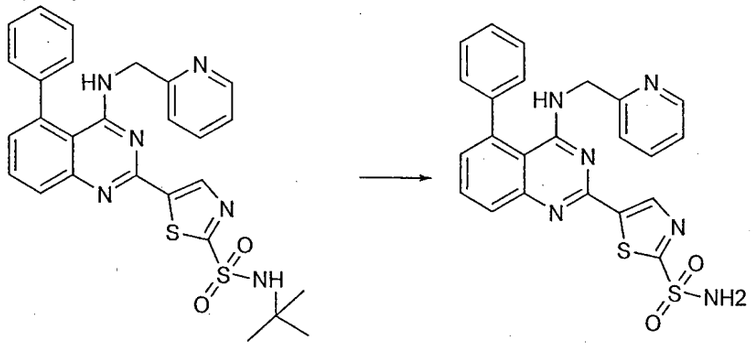
Etapa 3. Preparación de N-terc-butil-5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)tiazol-2-sulfonamida



A una suspensión en agitación de 5-bromo-N-terc-butiltiazol-2-sulfonamida (0,50 g, 1,67 mmol) en 1,4-dioxano (10 ml) se añadió cloruro de litio (0,210 g, 5,03 mmol), seguido por hexametildiestaño (0,820 g, 2,50 mmol).

Después de desgasificar con nitrógeno se añadió $Pd(TPP)_4$ (0,19 g, 0,16 mmol). La suspensión resultante se agitó durante la noche a temperatura ambiente. El compuesto 2-cloro-5-fenil-N-(piridin-2-ilmetil)quinazolin-4-amina (0,46 g, 1,33 mmol) se disolvió en 1,4-dioxano (3 ml) y después se añadió a la mezcla de reacción. Tras finalizar la adición, la mezcla de reacción se calentó a 90ºC durante 24 horas. Después de este tiempo, se evaporó el disolvente, se añadió agua y la mezcla se extrajo con DCM. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, se filtraron y se concentraron. El residuo resultante se purificó mediante recristalización con acetato de etilo y se purificó además mediante HPLC preparativa (procedimiento H) proporcionando N-terc-butil-5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)tiazol-2-sulfonamida (32 mg, 4,2 %) en forma de un sólido amarillo. CLEM Procedimiento V: Tr 2,47 min, [M+1] = 531,2; HPLC Procedimiento A1: pureza 97,3%, tiempo de retención = 10,89 min.

Etapa 4. Ejemplo 324



Una solución de N-terc-butil-5-(5-fenil-4-(piridin-2-ilmetilamino)quinazolin-2-il)tiazol-2-sulfonamida (0,03 g 0,05 mmol) en TFA (5

ml) se calentó a 80ºC durante 8 horas. Después de este tiempo se evaporó el TFA. La mezcla de reacción se basificó con 10% de solución de bicarbonato sódico y después se extrajo en DCM. Las capas orgánicas combinadas se secaron sobre Na_2SO_4, se filtraron y se concentraron dando un residuo. El residuo se purificó mediante recristalización con DCM/hexano proporcionando el Ejemplo 324 (23 mg, rendimiento de 86%) en forma de un sólido amarillo marronáceo. RMN ^{1}H (400 MHz, DMSO-d_6) δ: 8,68 (s, 1H); 8,21 (s, 1H); 8,19 (a s, 1H); 7,83-7,80 (m, 2h); 7,62 (dt, 1H, J = 1,6, 6,8 Hz); 7,61-7,49 (m, 5H); 7,32-7,28 (m, 2H); 7,23-7,20 (m, 1H); 6,94 (t, 1H, J = 4 Hz); 4,68 (d, 2H, J = 4 Hz). CLEM Procedimiento T: Tr 1,63 min, [M+1] = 475;0; HPLC Procedimiento A1: pureza 99,0 %, tiempo de retención = 8,05 min.

Se advierte que los ejemplos precedentes, aunque ilustrativos de la presente invención, no están en orden secuencial y puede faltar algún número de ejemplo.

UTILIDAD

En general, se ha demostrado que los compuestos de la presente invención, tal como los compuestos concretos divulgados en los ejemplos precedentes, inhiben la subfamilia K_v1 de los canales de K+ dependientes de voltaje (por ejemplo, mostrando valores % de inhibición $\geq$ 29%, preferentemente $\geq$ 30%, más preferentemente $\geq$ 40%, incluso más preferentemente $\geq$ 50%, a una concentración 0,3 micromolar en un ensayo como los que se exponen más adelante). Al mostrar actividad como inhibidores

de la subfamilia K_v1 de los canales de K+ dependientes de voltaje, cabe esperar que los compuestos de la presente invención sean útiles en el tratamiento de enfermedad humanas asociadas con la subfamilia K_v1 de canales de K+ dependientes de voltaje,

Los ensayos determinan el grado de actividad de un compuesto inhibidor de I_{Kur} se conocen bien en la técnica y se describen en referencias tales como *J. Gen. Physiol.*, 101(4):513-543 (Apr. 1993), and *Br. J. Pharmacol.*, 115(2):267-274 (May 1995).

Los ensayos para determinar el grado de actividad de un compuesto como inhibidor de otros miembros de la subfamilia K_v1 también se conocen bien en la técnica. Por ejemplo, la inhibición de $K_v1.1$, $K_v1.2$ y $K_v1.3$ se puede medir usando procedimientos descritos por by Grissmer, S. y col., *Mol. Pharmacol.*, 45(6):1227-1234 (Jun. 1994); la inhibición de $K_v1.4$ puede medirse usando procedimientos descritos por Petersen, K.R. y col., *Pflugers Arch.*, 437(3):381-392 (Feb. 1999); la inhibición de $K_v1.6$ se puede medir usando procedimientos descritos por Bowlby, M.R. y col., *J. Neurophysiol.* 73(6):2221-2229 (Jun. 1995); y la inhibición de $K_v1.7$ se puede medir usando procedimientos descritos por Kalman, K. y col., *J. Biol. Chem.*, 273(10):5851-5857 (Mar. 6, 1998).

Los compuestos de la presente invención se probaron en uno de los ensayos descritos justo en lo que antecede y se obtuvieron los resultados mostrados en la Tabla 2 siguiente.

Tabla 2

Ejemplo	Kv 1.5 (% inhibición a 0,3 uM)
7	95,7
22	60,4
29	65,3
31	98,2
32	53,1
38	61,3
40	59,8
42	96,4
46	98,7
50	96,1
97	98,7
105	98,7
107	50,3
108	98,1
110	51,8
111	61,5
130	96,2
134	98,4
137	55,6

En la Tabla 3 siguiente se exponen datos de los compuestos divulgados (véase la patente de EE.UU. Nº 7.713.983). Se cree que estos datos

demuestran la inesperada capacidad de los compuestos de la presente invención para incrementar significativamente la inhibición de la subfamilia K_v1 de canales de K+ dependientes de voltaje.

TABLA 3

Compuesto	Kv 1.5 (% inhibición a 0,3 uM)	Duplicados
Ejemplo 578 Documento US 7.713.983	20,5 ± 2,3	2
Ejemplo 580 Documento US 7.713.983	5,3 ± 5,1	2
Ejemplo 68 Documento US 7.713.983	8,5 ± 6,9	2
Ejemplo 82 Documento US 7.713.983	5,6 ± 3,8	2

Además, en los compuestos de la presente invención, tal como los compuestos concretos divulgados en los ejemplos precedentes, se evaluó su eficacia como inhibidores de la actividad del receptor de quinasa. Los compuestos se analizaron en el(los) ensayo(s) que se indican más adelante según la inhibición de la actividad quinasa y los resultados se muestran en la Tabla 4. Sobre estos resultados, se cree que los compuestos de la presente

invención, tal como los compuestos concretos divulgados en los ejemplos precedentes, no son eficaces en la inhibición de la actividad del receptor de quinasa y, por tanto, no serían eficaces como inhibidores o moduladores de la actividad del receptor de quinasa.

Ensayo de quinasa con Caliper

Los análisis se realizaron en placas de 384 pocillos de fondo en U. El volumen de ensayo final fue 30 µl preparados a partir de adiciones de 15 µl de enzima y sustratos (péptido con fluoresceína y ATP) y compuestos de ensayo en tampón de ensayo (HEPES 20 mM, Ph 7,4, $MgCl_2$ 10 Mm, 0,015% de Brij35 y DTT 4 mM. La reacción se inició mediante la combinación de proteína quinasa purificada con sustratos y compuestos de ensayo. La reacción se incubó a temperatura ambiente durante 60 minutos y se terminó mediante la adición a cada muestra de 30 µl de EDTA. La mezcla de reacción se analizó en el Caliper LABCHIP® 3000 (Caliper, Hopkinton, MA) mediante separación por electroforesis del sustrato fluorescente y el producto fosforilado. Los datos de inhibición se calcularon mediante comparación con reacciones de control sin enzima para 100% de inhibición y reacciones con sólo vehículo para 0% de inhibición. Se usó ATP a una concentración final equivalente a la Km y la concentración del sustrato peptídico fue 1,5 µM. Se generaron curves de respuesta a la dosis para determinar la concentración requerida para inhibir el 50% de la actividad quinasa (CI_{50}). Los compuestos se disolvieron a 10 mM en dimetilsulfóxido (DMSO) y se evaluaron a once concentraciones. Los valores de CI_{50} se obtuvieron por análisis de regresión no lineal.

TABLA 4

Ejemplo	LLE Flt3 (CI50, uM)	LLE GSK3B (CI50, uM)	LLE IGF1R (CI50, uM)	LLE IKKE (CI50, uM)	LLE IRAK-4 (CI50, uM)	LLE IRAK1 (CI50, uM)	LLE mAurA (CI50, uM)	LLE PIM1 (CI50, uM)	LLE_ABL1 (%INH, 50uM)	LLE_AURORA-B (CI50, uM)
1	—	50,00	—	50,00	50,00	50,00	—	—	—	50,00
7	—	50,00	—	—	50,00	—	—	—	—	—
19	10,11	5,15	17,58	50,00	18,69	—	39,84	33,81	32,37	—

Ejemplo	LLE_BMX (CI50, uM)	LLE_BTK (CI50, uM)	LLE_CDK2E (CI50, uM)	LLE_CDK5 (CI50, uM)	LLE_CDK5/p25 (CI50, uM)	LLE_CK1A1(CI50, uM)	LLE_CK2A1(CI50, uM)	LLE_CK2A2 (CI50, uM)	LLE_IGF1R (CI50, uM)	LLE_IRAK1 (CI50, uM)
1	50,00	50,00	50,00	—	—	—	—	—	—	50,00
7	50,00	50,00	50,00	—	—	—	—	50,00	—	—
19	—	19,17	50,00	50,00	50,00	50,00	50,00	25,52	17,58	—

001023

Ejemplo	LLE_ITK (CI50, uM)	LLE_JAK 1 (CI50, uM)	LLE_JAK 2 (CI50, uM)	LLE_JAK 3 (CI50, uM)	LLE_Lck (CI50, uM)	LLE_LYNA (CI50, uM)	LLE_mAur A (CI50, uM)	LLE_PIM1 (CI50, uM)	LLE_PLK 1 (CI50, uM)	LLE_SR C (CI50, nM)
1	50,00	—	23,87	50,00	50,00	50,00	—	—	—	—
7	50,00	—	50,00	50,00	50,00	50,00	—	—	—	—
19	—	50,00	17,79	23,84	—	—	39,84	33,81	50,00	50,00

Ejemplo	LLE_TAK1 (CI50, uM)	LLE_TBK1 (CI50, uM)	LLE_TEC (CI50, uM)	LLE_TPL2 CAL (CI50, uM)	LLE_TXK (CI50, uM)	LLE_TYK2_887 (CI50, uM)
1	50,00	50,00	50,00	—	50,00	50,00
7	—	—	50,00	—	—	50,00
19	—	—	—	11,90	—	50,00

001024

A la luz de lo anterior, se cree que los compuestos de la presente invención muestras inesperadas ventajas sobre los compuestos previamente divulgados en la técnica. Se cree que los compuestos de la presente invención demuestran una combinación deseable de la actividad inhibidora de la subfamilia K_v1 y mínima potencia contra las quinasas o los canales iónicos de Na+- Además, se cree que el Ejemplo 7 demuestra una combinación deseable de la actividad inhibidora de la subfamilia K_v1 y las características farmacológicas, incluido un sorprendentemente bajo grado de penetración en el cerebro en las especies en combinación con indicaciones de criterios de eficacia elevada y mejor seguridad, por ejemplo mejor selectividad por los canales iónicos medida en los estudios de hERG y canales de iones de Na+.

Los compuestos dentro del alcance de la presente inhibición inhiben la subfamilia K_v1 de canales de K+ dependientes de voltaje y, como tal, se cree que son útiles en el tratamiento y/o la prevención de diversos trastornos: arritmias cardíacas, incluidas las arritmias supraventriculares, arritmias auriculares, aleteo auricular, fibrilación auricular, complicaciones de isquemia cardíaca, y uso como agentes para controlar la frecuencia cardíaca; angina de pecho, incluidos alivio de los síntomas de Prinzmetal, síntomas vasoespásticos y síntomas variantes; trastornos gastrointestinales, incluidos esofagitis por reflujo, dispepsia funcional, trastornos de la motilidad (incluidos estreñimiento y diarrea) y síndrome del intestino irritable; trastornos del músculo liso vascular y visceral, incluidos asma, enfermedad pulmonar obstructiva crónica, síndrome de dificultad respiratoria del adulto, enfermedad vascular periférica (incluida la claudicación intermitente), insuficiencia venosa, impotencia, espasmo cerebral y coronario, y enfermedad de Raynaud; enfermedad inflamatoria e

inmunológica, incluidas enfermedad intestinal inflamatoria, artritis reumatoide, rechazo de injerto, asma, enfermedad pulmonar obstructiva crónica, fibrosis quística y aterosclerosis; trastornos de la proliferación celular, incluidos reestenosis y cáncer (incluida la leucemia); trastornos del sistema de audición; trastornos del sistema visual, incluida degeneración macular y cataratas; diabetes, incluidas retinopatía diabética, nefropatía diabética; enfermedades musculares, incluidos miotonía y emaciación; neuropatía periférica; trastornos de la cognición; migraña; pérdida de memoria, incluidas enfermedad de Alzheimer y demencia; disfunción motora mediada por el SNC, incluidas enfermedad de Parkinson y ataxia; epilepsia y otros trastornos mediados por los canales iónicos.

Como inhibidores de la subfamilia K_v1 de canales de K+ dependientes de voltaje, se cree que los compuestos de la presente invención son útiles para tratar una variedad de otros trastornos, incluyendo resistencia al transplante de órganos o tejidos, enfermedades del injerto contra el huésped causadas por transplantes de médula ósea, artritis reumatoide, lupus eritematoso sistémico, tiroiditis de Hashimoto, esclerosis múltiple, miastenia gravis, diabetes de tipo I, uveítis, diabetes mellitus de inicio en la juventud o de inicio reciente, uveítis posterior, encefalomielitis alérgica, glomerulonefritis, enfermedades infecciosas causadas por microorganismos patogénicos, enfermedades cutáneas inflamatorias e hiperproliferativas, psoriasis, dermatitis atópica, dermatitis por contacto, dermatitis eccematosa, dermatitis seborreica, liquen plano, pénfigo, penfigoide bulloso, epidermolisis bullosa, urticaria, angioedemas, vasculitis, eritemas, eosinofilias cutáneas, lupus eritematoso, acné, alopecia areata, queratoconjuntivitis, conjuntivitis vérnica, uveítis

asociada con la enfermedad de Behcet, queratitis, queratitis herpética, córnea cónica, distrofia epitelial corneal, leucoma corneal, pénfigo ocular, úlcera de Mooren, escleritis, oftalmopatía de Graves, síndrome de Vogt-Koyanagi-Harada, sarcoidosis, alergias al polen, enfermedad obstructiva de las vías aéreas reversible, asma bronquial, asma alérgico, asma intrínseco, asma extrínseco, asma por polvo, asma crónica o incurable, asma tardía e hiperrespuesta de las vías aéreas, bronquitis, úlceras gástricas, daños vasculares causados por enfermedades isquémicas y trombosis, enfermedad intestinal isquémica, enfermedades intestinales inflamatorias, enterocolitis necrotizante, lesiones intestinales asociadas con quemaduras térmicas, enfermedades mediadas por el leucotrieno B4, enfermedades celíacas, proctitis, gastroenteritis eosinófila, mastocitosis, enfermedad de Crohn, colitis ulcerosa, migraña, rinitis, eccema, nefritis intersticial, síndrome de Goodpasture, síndrome hemolítico-urémico, nefropatía diabética, miositis múltiple, síndrome de Guillain-Barre, enfermedad de Meniere, polineuritis, neuritis múltiple, mononeuritis, radiculopatía, hipertiroidismo, enfermedad de Basedow, aplasia pura de glóbulos rojos, anemia aplásica, anemia hipoplásica, púrpura trombocitopénica idiopática, anemia hemolítica autoinmunitaria, agranulocitosis, anemia perniciosa, anemia megaloblástica, aneritroplasia, osteoporosis, sarcoidosis, pulmón fibroide, neumonía intersticial idiopática, dermatomiositis, leucoderma vulgar, ictiosis vulgar, sensibilidad fotoalérgica, linfoma cutáneo de células T, arteriosclerosis, aterosclerosis, síndrome de aortitis, poliarteritis nodosa, miocardosis, esclerodermia, granuloma de Wegener, síndrome de Sjögren, adiposis, fascitis eosinófila, lesiones de la encía, periodontio, hueso alveolar, substantia ossea dentis, glomerulonefritis,

alopecia de patrón masculino o alopecia senil previniendo la depilación o proporcionando la germinación de pelo y/o estimulando la generación de pelo y el crecimiento de pelo, distrofia muscular, pioderma y síndrome de Sezary, enfermedad de Addison, lesión isquémica por reperfusión de órganos que se produce tras conservación, transplante o enfermedad isquémica, shock endotóxico, colitis seudomembranosa, colitis causada por fármacos o radiación, insuficiencia renal isquémica aguda, insuficiencia renal crónica, toxinosis causada por oxigeno o fármacos en los pulmones, cáncer de pulmón, enfisema pulmonar, cataratas, siderosis, retinitis pigmentosa, degeneración macular senil, cicatrización vítrea, quemadura alcalina corneal, dermatitis eritema multiforme, dermatitis bullosa lineal por IgA y dermatitis cemento, gingivitis, periodontitis, sepsis, pancreatitis, enfermedades causadas por la contaminación ambiental, envejecimiento, carcinogénesis, metástasis de carcinoma e hipobaropatía, enfermedad causada por liberación de histamina o leucotrieno C_4, enfermedad de Behcet, hepatitis autoinmunitaria, cirrosis biliar primaria, colangitis esclerosante, resección hepática parcial, necrosis hepática aguda, necrosis causada por toxinas, hepatitis viral, shock o anoxia, hepatitis por el virus B, hepatitis no A/no B, cirrosis, cirrosis alcohólica, insuficiencia hepática, insuficiencia hepática fulminante, insuficiencia hepática de inicio tardío, insuficiencia hepática "aguda o crónica", aumento del efecto quimioterapéutico, infección por citomegalovirus, infección por HCMV, SIDA, cáncer, demencia senil, traumatismo e infección bacteriana crónica.

Los compuestos de la presente invención son posibles agentes antiarrítmicos que son útiles en la prevención y el tratamiento (incluido el alivio parcial o la curación) de arritmias. Como inhibidores de $K_v1.5$, los compuestos

dentro del alcance de la presente invención son particularmente útiles en la prevención y tratamiento selectivos de las arritmias supraventriculares, tales como fibrilación auricular y aleteo auricular. Por "prevención y tratamiento selectivos de las arritmias supraventriculares" se quiere decir la prevención o el tratamiento de arritmias supraventriculares en las que la proporción entre la prolongación del periodo refractario efectivo auricular y la prolongación del periodo refractario efectivo ventricular es superior a 1:1. Esta proporción también puede ser mayor que 4:1, incluso mayor que 10:1. Además, la proporción puede ser tal que la prolongación del periodo de respuesta refractario efectivo auricular se consigue sin una prolongación significativamente detectable del periodo refractario efectivo ventricular.

Además, los compuestos dentro del alcance de la presente invención bloquean I_{Kur} y, por tanto, pueden ser útiles en la prevención y el tratamiento de todas las afecciones asociadas con la I_{Kur}. Una "afección asociada con la I_{Kur}" es un trastorno que puede evitarse, aliviarse parcialmente o curarse mediante la administración de un bloqueante de I_{Kur}. Se sabe que el gen de $K_v1.5$ se expresa en tejido estomacal, tejido intestinal/de colon, arterias pulmonares y en las células pancreáticas beta. Por tanto, la administración de un bloqueante de I_{Kur} puede proporcionar tratamiento útil para trastornos tales como: esofagitis por reflujo, dispepsia funcional, estreñimiento, asma y diabetes. Además, se sabe que $K_v1.5$ se expresa en la adenohipófisis. Por tanto, la administración de un bloqueante de I_{Kur} puede estimular la secreción de hormona del crecimiento. Adicionalmente, los inhibidores de I_{Kur} pueden ser útiles en los trastornos de proliferación celular, tales como leucemia, y enfermedades autoinmunitarias, tales como artritis reumatoide y rechazo de

transplantes.

Por tanto, la presente invención proporciona procedimientos para la prevención o el tratamiento de uno o más de los trastornos mencionados en lo que antecede, que comprenden la etapa de administrar a un sujeto que lo necesite una cantidad eficaz de al menos un compuesto de la fórmula I, Ia, Ib y/o Ic, preferentemente compuestos ejemplificados en los ejemplos, más preferentemente los Ejemplos 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 y 137, incluso más preferentemente los Ejemplos 7, 32 y 101, todavía más preferentemente los ejemplos 7 y 101. Otros agentes terapéuticos tales como los descritos más adelante pueden emplearse con los compuestos de la invención en los presentes procedimientos. En los procedimientos de la presente invención, dicho(s) otro(s) agente(s) terapéutico(s) pueden administrarse antes, de forma simultánea o después de la administración del(los) compuesto(s) de la presente invención.

DOSIFICACIÓN Y FORMULACIÓN

La presente invención también proporciona composiciones farmacéuticas que comprenden al menos uno de los compuestos de la fórmula I, Ia, Ib y/o Ic, preferentemente compuestos ejemplificados en los ejemplos, más preferentemente los Ejemplos 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 y 137, incluso más preferentemente los Ejemplos 7, 32 y 101, todavía más preferentemente los ejemplos 7 y 101, o sales de los mismos capaces de prevenir o tratar uno o más de los trastornos mencionados en lo que antecede en una cantidad eficaz de los mismos y un vehículo o diluyente farmacéuticamente aceptable. Las composiciones de la

presente invención pueden contener otros agentes terapéuticos tal como los descritos más adelante y pueden formularse, por ejemplo, empleando vehículos o diluyentes sólidos o líquidos convencionales, así como aditivos farmacéuticos de un tipo adecuado al modo de administración deseado (por ejemplo, excipientes, aglutinantes, conservantes, estabilizantes, sabores, etc.) de acuerdo con técnicas tales como las bien descritas en la técnica de la formulación farmacéutica.

Los compuestos de la fórmula I, Ia, Ib y/o Ic, preferentemente los compuestos ejemplificados en los ejemplos, más preferentemente en los Ejemplos 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 y 137, incluso más preferentemente en los Ejemplos 7, 32 y 101, todavía más preferentemente en los ejemplos 7 y 101, se pueden administrar por cualquier medio adecuado, por ejemplo por vía oral, tal como en forma de comprimidos, cápsulas, gránulos o polvos; sublingual: bucal; parenteral, tal como mediante inyección subcutánea, intravenosa, intramuscular o intraesternal, o técnicas de infusión (*p. ej.*, en forma de soluciones o suspensiones inyectables acuosas o no acuosas); por vía nasal, tal como pulverizador nasal; por vía tópica, tal como en forma de una crema o ungüento; o por vía rectal, tal como en forma de supositorios; en formulaciones monodosis que contienen vehículos o diluyentes farmacéuticamente aceptables. Los presentes compuestos pueden administrarse, por ejemplo, en una forma adecuada para la liberación inmediata o la liberación prolongada. La liberación inmediata o la liberación prolongada se pueden conseguir mediante el uso de composiciones farmacéuticas adecuadas que comprenden los presentes compuestos o, particularmente en el caso de la liberación

prolongada, mediante el uso de dispositivos tales como implantes subcutáneos o bombas osmóticas. En el caso en el que los compuestos de fórmula I, Ia, Ib y/o Ic, preferentemente los compuestos ejemplificados en los ejemplos, más preferentemente en los Ejemplos 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 y 137, incluso más preferentemente en los Ejemplos 7, 32 y 101, todavía más preferentemente en los ejemplos 7 y 101, se estén administrando para prevenir o tratar arritmias, los compuestos se pueden administrar para conseguir conversión química al ritmo sinusal normal u, opcionalmente, pueden usarse junto con cardioconversión eléctrica.

Composiciones de ejemplo para administración oral incluyen suspensiones que pueden contener, por ejemplo, celulosa microcristalina para impartir BULK, ácido algínico o alginato sódico como agente de suspensión, metilcelulosa como potenciador de la viscosidad, y agentes edulcorantes o aromatizantes tales como los conocidos en la técnica; y comprimidos de liberación inmediata, que pueden contener, por ejemplo, celulosa microcristalina, fosfato dicálcico, almidón, estearato de magnesio y/o lactosa y/u otros excipientes, aglutinantes, expansores, disgregantes, diluyentes y lubricantes, tales como los conocidos en la técnica. Los compuestos de fórmula I, Ia, Ib y/o Ic, preferentemente los compuestos ejemplificados en los ejemplos, más preferentemente en los Ejemplos 7, 22, 29, 31, 32, 38, 40, 42, 46, 50, 97, 105, 107, 108, 110, 111, 130, 134 y 137, incluso más preferentemente en los Ejemplos 7, 32 y 101, todavía más preferentemente en los ejemplos 7 y 101, también se pueden administrar a través de la cavidad oral mediante administración sublingual y/o bucal. Formas de ejemplo que se pueden usar son pastillas moldeadas, comprimidos o pastillas liofilizadas.

Entre las composiciones de ejemplo se incluyen las que formulan el(los) compuesto(s) presente(s) con diluyentes de disolución rápida tales como manitol, lactosa, sacarosa y/o ciclodextrinas. También incluidos en dichas formulaciones pueden estar los excipientes de alto peso molecular tales como celulosas (AVICEL®) o polietilenglicoles (PEG). Dichas formulaciones pueden también incluir un excipiente para ayudar a la adhesión a las mucosas, tal como hidroxipropilcelulosa (HOC), hidroxipropilmetilcelulosa (HPMC), carboximetilcelulosa sódica (SCMC), copolímero de anhídrido maleico (*p. ej.*, Gantrez) y agentes para controlar la liberación tales como copolímero poliacrílico (*p. ej.*, Carbopol 934). También se pueden añadir lubricantes, deslizantes, sabores, agentes colorantes y estabilizantes para facilidad de fabricación y uso.

Entre las composiciones de ejemplo para administración nasal por aerosol o inhalación se incluyen soluciones en solución salina que pueden contener, por ejemplo, alcohol bencílico, u otros conservantes adecuados, estimulantes de la absorción para potenciar la biodisponibilidad, y/o otros agentes de solubilización o dispersión tales como los conocidos en la técnica.

Entre las composiciones de ejemplo para administración parenteral se incluyen soluciones o suspensiones inyectables que pueden contener, por ejemplo, diluyentes o disolventes no tóxicos parenteralmente aceptables, tales como manitol, 1,3-butanodiol, agua, solución de Ringer, una solución de cloruro sódico isotónico, u otros agentes de suspensión, dispersión o humidificación adecuados, incluidos mono o diglicéridos sintéticos, y ácidos grasos, incluido el ácido oleico.

Entre los ejemplos de composiciones para administración rectal se

incluyen supositorios, que pueden contener, por ejemplo, un excipiente no irritante adecuado, tal como manteca de cacao, ésteres glicéridos sintéticos o polietilenglicoles, que son sólidos a las temperaturas habituales pero que se funden y/o disuelven en la cavidad rectal para liberar el fármaco.

Entre los ejemplos de composiciones para administración tópica se incluyen un transportador tópico, tal como Plastibase (aceite mineral gelificado con polietileno).

Un experto en la técnica puede determinar la cantidad eficaz de un compuesto de la presente invención e incluye cantidades de dosificación de ejemplo para un humano adulto de aproximadamente 0,001 a 100 mg/kg de peso corporal del compuesto activo al día, que se puede administrar en una dosis única o en forma de dosis divididas individuales, tal como de 1 a 4 veces al día. Debe entenderse que el nivel de dosis y la frecuencia de las dosis específicos para cualquier sujeto particular puede variar y dependerá de una variedad de factores que incluyen la actividad del compuesto específico que se emplee, la estabilidad metabólica y duración de la acción de ese compuesto, la especie, la edad, el peso corporal, el estado de salud general, el sexo y la dieta del sujeto, el modo y el momento de la administración, la tasa de excreción, la combinación de fármacos y la gravedad de la afección concreta. Sujetos preferidos para el tratamiento incluyen animales, más preferentemente especies de mamífero tales como seres humanos, y animales domésticos tales como perros, gatos y similares, sujetos a los trastornos mencionados en lo que antecede.

Los compuestos de la presente invención pueden emplearse solos o en combinación unos con otros y/o otros agentes terapéuticos útiles en el

tratamiento de los trastornos mencionados en lo que antecede y otros trastornos, incluidos: Otros agentes antiarrítmicos, tales como agentes de clase I (*p. ej.*, propafenona), agentes de clase II (*p. ej.*, carvadiol y propranolol), agentes de clase III (*p.ej.*, sotalol, dofetilida, amiodarona, azimilida e ibutilida), agentes de clase IV (*p.ej.*, diltiazem y verapamilo), antagonistas de 5HT (*p.ej.*, sulamserod, serralina y tropsetron), y dronedarona; bloqueantes de los canales de calcio (tanto de tipo L como de tipo T) tal como diltiazem, verapamilo, nifedipina, amlodipina y mybefradil; inhibidores de la ciclooxigenasa (*es decir,* inhibidores de la COX-1 y/o la COX-2) tal como aspirina, indometacina, ibuprofeno, piroxicam, naproxeno, CELEBREX®, VIOXX® y AINE; agentes antiplaquetarios tal como bloqueantes de GPIIb/IIIa (*p.ej.*, abciximab, eptifibatide y tirofiban), antagonistas de P2Y12 (*p.ej.*, clopidogrel, cangrelor, ticlopidina y CS-747), antagonistas de P2Y1, antagonistas del receptor de tromboxano (*p.ej.*, ifetroban), aspirina e inhibidores de la PDE-III (*p.ej.*, dipiridamol) con o sin aspirina; diuréticos tales como clorotiazida, hidroclorotiazida, flumetiazida, hidroflumetiazida, bendroflumetiazida metilclorotiazida, triclorometiazida, politiazida, benztiazida, ácido etacrínico tricrinafeno, clortalidona, furosemida, musolimina, bumetanida, triamtreneno, amilorida, y espironolactona; agentes antihipertensores tales como bloqueantes alfa adrenérgicos, bloqueantes beta adrenérgicos, bloqueantes de los canales de calcio, diuréticos, inhibidores de la renina, inhibidores de la ECA, (*p.ej.*, captropril, zofenopril, fosinopril, enalapril, ceranopril, cilazopril, delapril, pentopril, quinapril, ramipril, lisinopril), antagonistas de la A II (*p.ej.*, losartán, irbesartán, valsartán), antagonistas de ET (*p.ej.*, sitaxentán, atrasentán y compuestos divulgados en las patentes de EE.UU. Nº 5.612.359 y

6.043.265), antagonistas dobles de ET/AII (*p.ej.*, compuestos divulgados en el documento WO 00/01389), inhibidores de la endopeptidasa neural (NEP), inhibidores de la vasopepsidasa (inhibidores dobles de NEP-ECA) (*p.ej.*, omapatrilat y gemopatrilat), nitratos, y combinaciones de dichos agentes antihipertensores; agentes antitrombóticos/trombolíticos tales como el activador de plasminógeno tisular (tPA), tPA recombinante, tenecteplasa (TNK), lanoteplasa (nPA), inhibidores del factor VIIa, inhibidores del factor Xa (tal como razaxaban), inhibidores del XIa, inhibidores de la trombina (*p.ej.*, hirudina y argatroban), inhibidores de PAI-1 (*es decir.*, inactivadores de los inhibidores del activador de plasminógeno tisular), inhibidores de la α2-antiplasmina, estreptoquinasa, uroquinasa, prouroquinasa, complejo activador de estreptoquinasa plasminógeno anisolado, y activadores del plasminógeno de glándulas salivares o animales; anticoagulantes tales como warfarina y heparinas (incluidas las heparinas sin fraccionar y de bajo peso molecular, tal como enoxaparina y dalteparina); inhibidores de la HMG-CoA reductasa tales como pravastatina lovastatina, atorvastatina, simvastatina, NK-104 (a.k.a. itavastatina o nisvastatina o nisbastatina) y ZD-4522 (a.k.a. rosuvastatina o atavastatina o visastatina); otros agentes reductores del colesterol/lípidos tales como inhibidores de escualeno, fibratos, y secuestrantes de ácidos biliares (*p.ej.*, QUESTRAN®); agentes antipoliferativos tales como ciclosporina A, TAXOL®, FK 506, y adriamicina; agentes antitumorales tales como TAXOL®, adriamicina, epotilonas, cisplatino y carboplatino; agentes antidiabéticos tales como biguanidas (*p.ej.*, metformina), inhibidores de la glucosidasa (*p.ej.*, acarbosa), insulinas, meglitinidas (*p.ej.*, repaglinida), sulfonilureas (*p.ej.*, glimepirida, gliburida y glipizida), combinaciones biguanida/gliburida (*es decir.*,

GLUCOVANCE®), tiozolidinadionas (*p.ej.*, troglitazona, rosiglitazona y pioglitazona), agonistas de PPAR-gamma, inhibidores de aP2 e inhibidores de DP4; miméticos tiroideos (incluidos los antagonistas del receptor tiroideo) (*p.ej.*, tirotropina, politiroide, KB-130015, y dronedarona); antagonistas de los receptores mineralocorticoides, tales como espironolactona y eplerinona; secretagogos de la hormona del crecimiento; agentes antiosteoporóticos (*p.ej.*, alendronato y raloxifeno); agentes de terapia de sustitución hormonal tales como estrógenos (incluidos los estrógenos conjugados en premarina), y estradiol; antidepresivos tales como nefazodona y sertralina; agentes antiansiedad tales como diazepam, lorazepam, buspirona y pamoato de hidroxizina; anticonceptivos orales; agentes antiulcerosos y para la enfermedad del reflujo gastroesofágico tales como famotidina, ranitidina y omeprazol; agentes antiobesidad tales como orlistat; glicósidos cardíacos incluidos digitálicos y ouabaína; inhibidores de la fosfodiesterasa, incluidos los inhibidores de la PDE III (*p.ej.*, cilostazol), e inhibidores de la PDE V (*p.ej.*, sildenafil); inhibidores de la proteína tirosina quinasa; agentes antiinflamatorios esteroideos tales como prednisona y dexametasona; y otros agentes antiinflamatorios tales como ENBREL®. Las combinaciones se pueden co-formular o en forma de kit envasados proporcionando dosificaciones adecuadas para co-administración.

Los otros agentes terapéuticos anteriores, cuando se emplean en combinación con los compuestos de la presente invención, se pueden usar en, por ejemplo, las cantidades indicadas en el Physicians' Desk Reference (PDR) o como determine un experto en la técnica.

Publicaciones y referencias, incluidos, entre otros, patentes y

solicitudes de patentes, que se citan en la presente memoria descriptiva se incorporan en el presente documento por referencia en su totalidad en toda la porción citada como si cada publicación o referencia individual estuviera individual y específicamente indicada para su incorporación en el presente documento por referencia como expuesta completamente. Cualquier solicitud de patente a la que esta solicitud reivindica prioridad también se incorpora en el presente documento por referencia del modo descrito en lo que antecede para publicaciones y referencias.

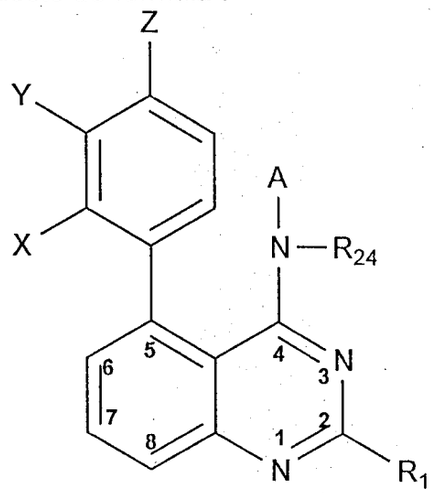
Aunque la presente invención se ha descrito haciendo énfasis en formas de realización concretas, será obvio para los expertos en la técnica que se pueden usar variaciones en los compuestos y procedimientos concretos y que se pretende que la invención se ponga en práctica de otros modos distintos a los específicamente descritos en el presente documento. De acuerdo con esto, la presente invención incluye todas las modificaciones abarcadas dentro del espíritu y alcance de la invención, tal como se define en las reivindicaciones siguientes.

001039

Habiendo descrito la invención como antecede, se declara como propiedad lo contenido en las siguientes

REIVINDICACIONES

1. Un compuesto de fórmula I



I

o un enantiómero, diastereómero, tautómero o sales del mismo, en la que:

X es H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-NR_{11}SO_2R_{12}$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-NR_{11}SO_2NR_{11}R_{12}$, $-OCONR_{11}R_{12}$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Y es H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-NR_{11}SO_2NR_{11}R_{12}$, $-OCONR_{11}R_{12}$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

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Z es H, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 6 a 12 miembros, heterociclilo de 4 a 12 miembros, $-NO_2$, $-NR_{11}SO_2R_{12}$, $-SO_2NR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-NR_{11}SO_2NR_{11}R_{12}$, $-OCONR_{11}R_{12}$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

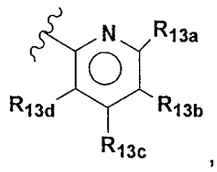
A es $-(CH_2)_m-R_2$, $-CH(R_{25})(R_{26})$, $-CH(R_{26})-CO_2-R_{2a}$ o $-(CH_2)_{n-1}-NR_{25}-CO_2-R_{24}$;

m es 0 a 4;

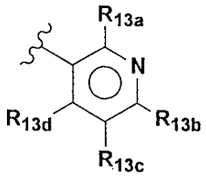
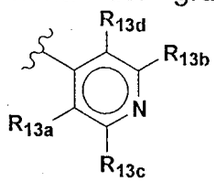
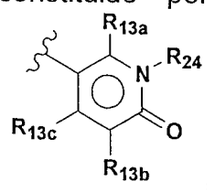
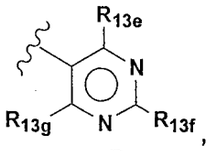
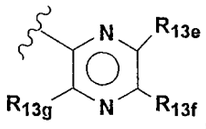
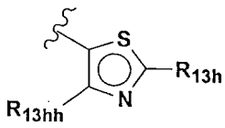
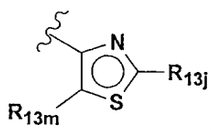
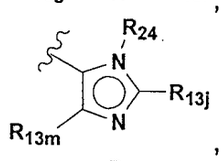
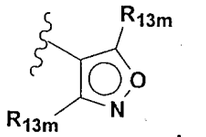
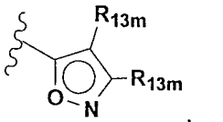
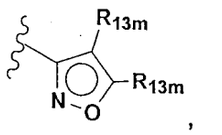
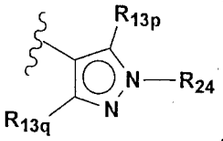
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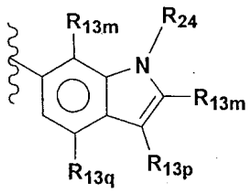
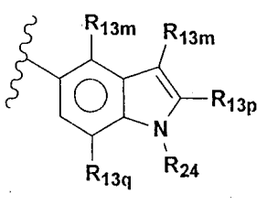
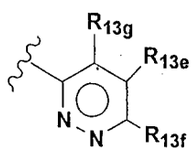
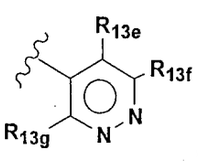
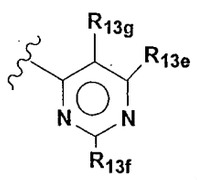
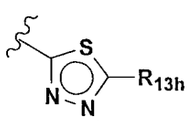
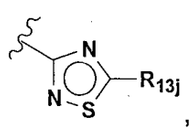
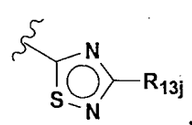
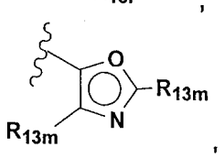
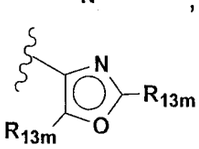
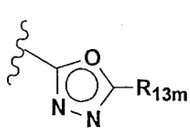
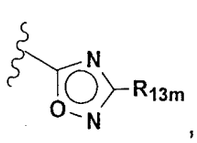
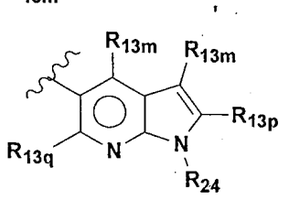
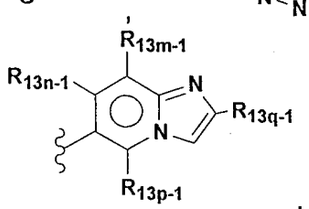
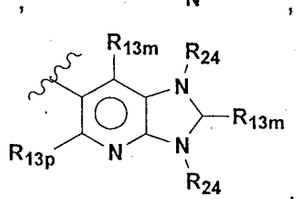
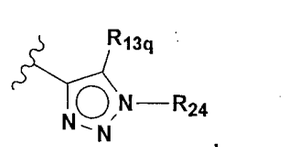
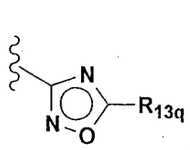
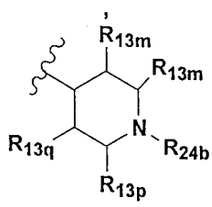
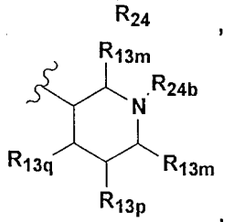
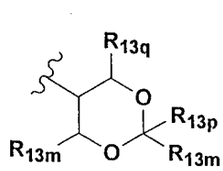
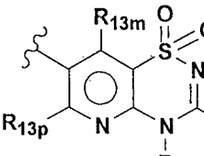
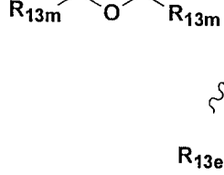
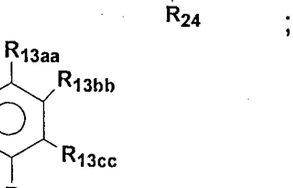
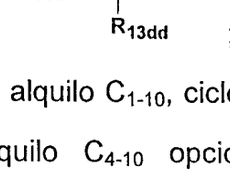
n-1 es 2 a 4;

R_1 es -OH, F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, cicloalquilo C_{3-10}, -CN, $-(CH_2)_n-SO_2NR_{11}R_{12}$, $-(CH_2)_n-CO_2R_{11}$ o $-(CH_2)_n-NR_{11}SO_2R_{12}$, pudiendo estar el alquenilo y cicloalquilo opcionalmente sustituidos con uno o más R_{13}; o



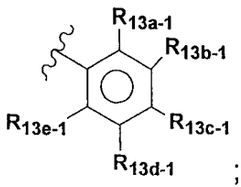
R_1 se selecciona del grupo constituido por:


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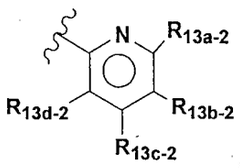
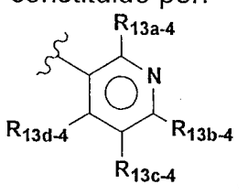
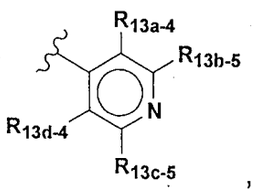
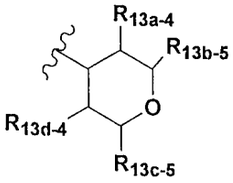
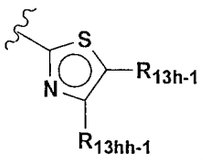
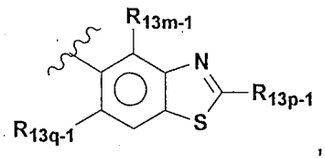
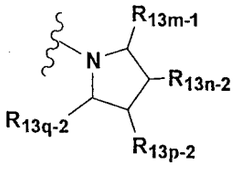
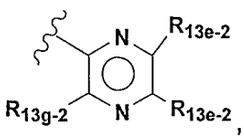
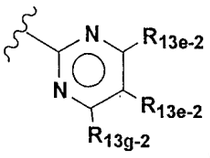
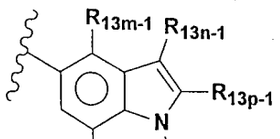
R_1 es ;

R_2 es alquilo C_{1-10}, ciclopropilo opcionalmente sustituido con uno o más R_{13}; cicloalquilo C_{4-10} opcionalmente sustituido con uno o más R_{13bb}; cicloalquenilo C_{3-10} opcionalmente sustituido con uno o más R_{13b}; o $-NR_{14}R_{14}$; con la condición de que R_2 no sea $-NR_{14}R_{14}$ cuando m sea 0, 1 ó 3; o



R_2 es ; o

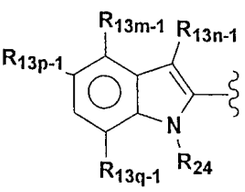
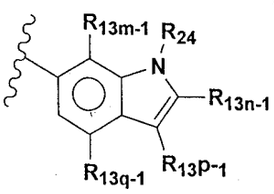
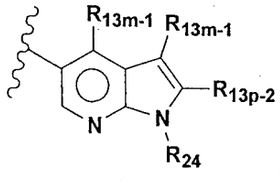
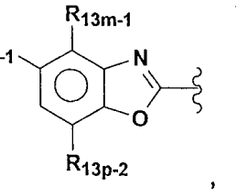
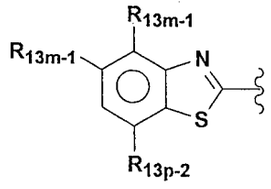
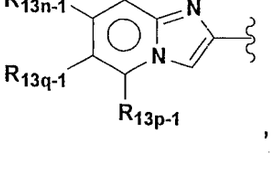
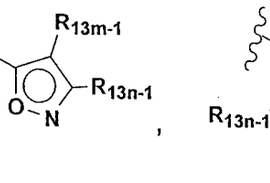
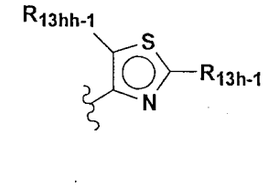
R_2 se selecciona del grupo constituido por:


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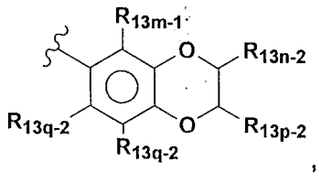
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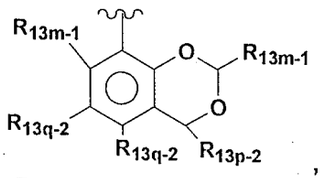
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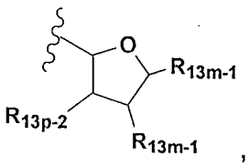
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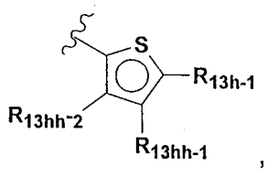
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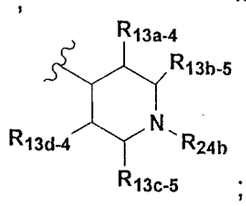
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R_{2a} es alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, $-NR_{14}R_{14}$, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, cualquiera de los cuales está opcionalmente sustituido con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{11} y R_{12}, en cada aparición, se seleccionan independientemente de H, alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros y un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

R_{11} y R_{12} se toman junto con el nitrógeno al que están unidos formando un heterociclilo de 4 a 12 miembros, pudiendo estar el heterociclilo opcionalmente sustituido con uno o más R_{13} y el heterociclilo está constituido por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I,

alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; con la condición de que cuando R_{13} sea alquilo sustituido con un R_{14a}, R_{14a} no sea -OH;

R_{13a}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N,

S u O;

R_{13aa}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y

1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2}, en cada aparición, es independientemente H, -OH, F, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más

001047

R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13bb}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y

heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$,

pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, -

$CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-(CH_2)_n-OCONR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13cc}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, -

$CONR_{14}OR_{14}$, o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 6 a 12 miembros, un heterociclilo de 6 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, $-NO_2$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-NR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo,

alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-4}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, -

$CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13dd}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, -

001054

$NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, -

$NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, -

$NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13ee}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-1}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, -

$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13f}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-

$NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, -

$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13h}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13h-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{7-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de

4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$, -$C(=NOR_{14})NR_{14}R_{14}$, -$CONR_{14}OR_{14}$ o -$NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12},

alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13j}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I,

alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13m}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13m-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13n-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo

constituido por N, S u O;

R_{13p}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13p-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y

1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13p-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más

R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$, $-CONR_{14}OR_{14}$ o $-NCOR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo,

alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{14} se toman junto con los átomos a los que están unidos formando un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-NO_2$, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, =O, $-CONR_{24}R_{24}$, $-COR_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$, $-NR_{24}CO_2R_{24}$, $-SO_2NR_{24}R_{24}$, o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12

miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{24} se toman junto con los átomos a los que están unidos formando un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, =O, $-CONR_{25}R_{25}$, $-COR_{25}$, $-NR_{25}R_{25}$, $-NR_{25}CO_2R_{25}$, o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24b}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, $-CO_2R_{25}$, $-SO_2NR_{25}R_{25}$, $-COR_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y

heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

con la condición de que:

(i) R_1 no sea Cl cuando m sea 0, 1 ó 2; R_{13a-1} es H, $-CF_3$, o metoxi; R_{13c-1} sea H, OH, metoxi o dimetilamino; X, Y, Z, R_{13b-1}, R_{13d-1}, R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d-2}, R_{13e-2}, R_{13g-2}, R_{13a-4}, R_{13b-4}, R_{13c-4}, R_{13d-4}, R_{13b-5}, R_{13c-5}, R_{13m-1}, R_{13n-1}, R_{13p-1} y R_{13q-1} sean H; y

(ii) m no sea 0 ó 1 cuando X, Y, R_{13a}, R_{13d}, R_{13e}, R_{13g}, R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d-2}, R_{13a-4}, R_{13b-4}, R_{13c-4}, R_{13d-4} R_{13b-5}, R_{13c-5}, R_{13h-1} y R_{13hh-1} sean H; R_{13b} es H o $-SO_2NH_2$; R_{13c} sea H, $-CONH_2$, $-SO_2N(C_2H_4OH)_2$, $-SO_2NHCOCH_3$, $-SO_2NH_2$, -tetrazolilo o (4-aminopiperidinil)sulfonilo; R_{13f} sea H o $-NHC_2H_4OCH_3$; y Z sea H, $-CO_2H$, o $-CO_2CH_3$.

2. El compuesto, enantiómero, diastereómero, tautómero o sal del mismo, de la reivindicación 1, en el que:

X es H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Y es H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo

C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-SO_2NR_{11}R_{12}$, $-CONR_{11}R_{12}$, $-NR_{11}CONR_{11}R_{12}$, $-NCOR_{11}$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Z es H, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 6 a 12 miembros, heterociclilo de 4 a 12 miembros, $-NO_2$, $-SO_2NR_{11}R_{12}$, $-NCOR_{11}$, $-NR_{11}SO_2NR_{11}R_{12}$, $-OCONR_{11}R_{12}$ o $-NR_{11}R_{12}$;

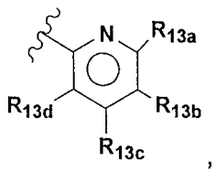
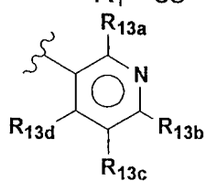
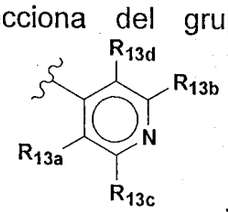
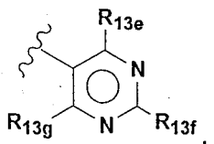
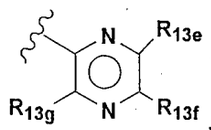
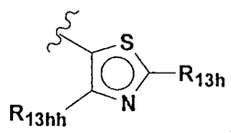
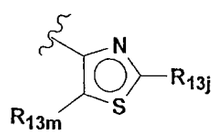
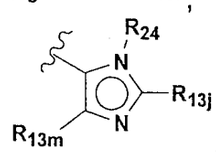
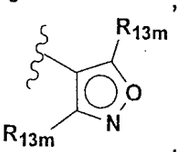
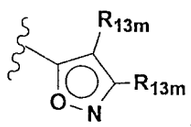
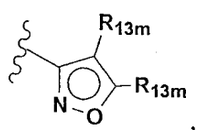
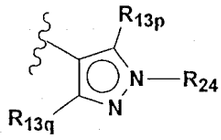
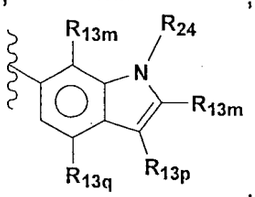
A es $-(CH_2)_m-R_2$, $-CH(R_{25})(R_{26})$ o $-CH(R_{26})-CO_2-R_{2a}$;

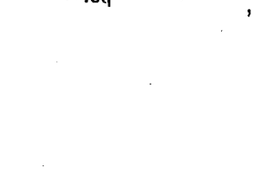
m es 0 a 4;

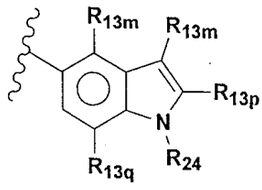
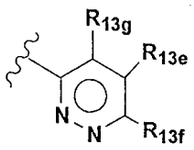
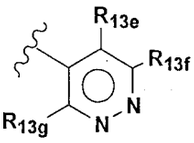
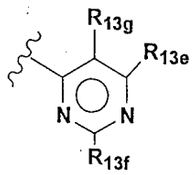
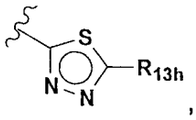
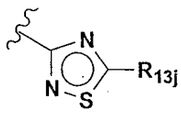
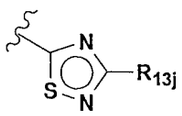
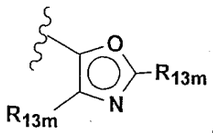
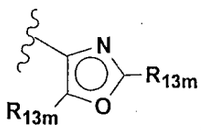
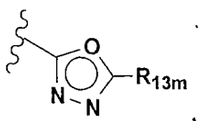
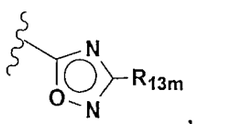
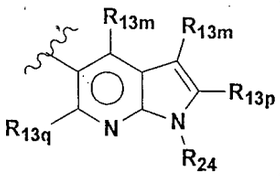
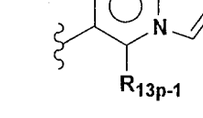
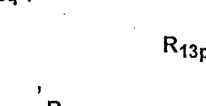
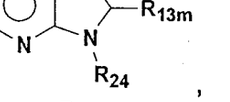
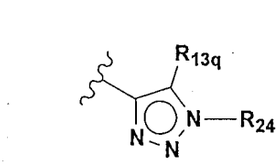
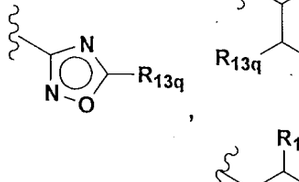
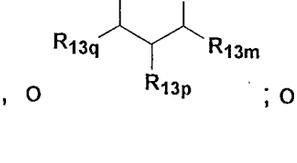
n es 1 a 4;

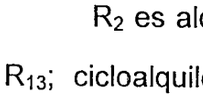
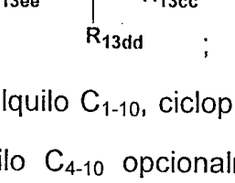
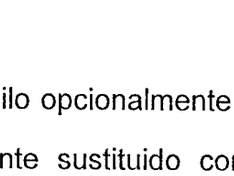
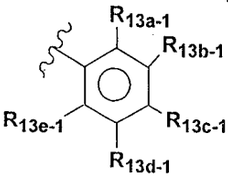
R_1 es -OH, F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, cicloalquilo C_{3-10}, -CN, $-(CH_2)_n-SO_2NR_{11}R_{12}$ o $-(CH_2)_n-NR_{11}SO_2R_{12}$, pudiendo estar el alquenilo y cicloalquilo opcionalmente sustituidos con uno o más R_{13}; o

R_1 se selecciona del grupo constituido por:

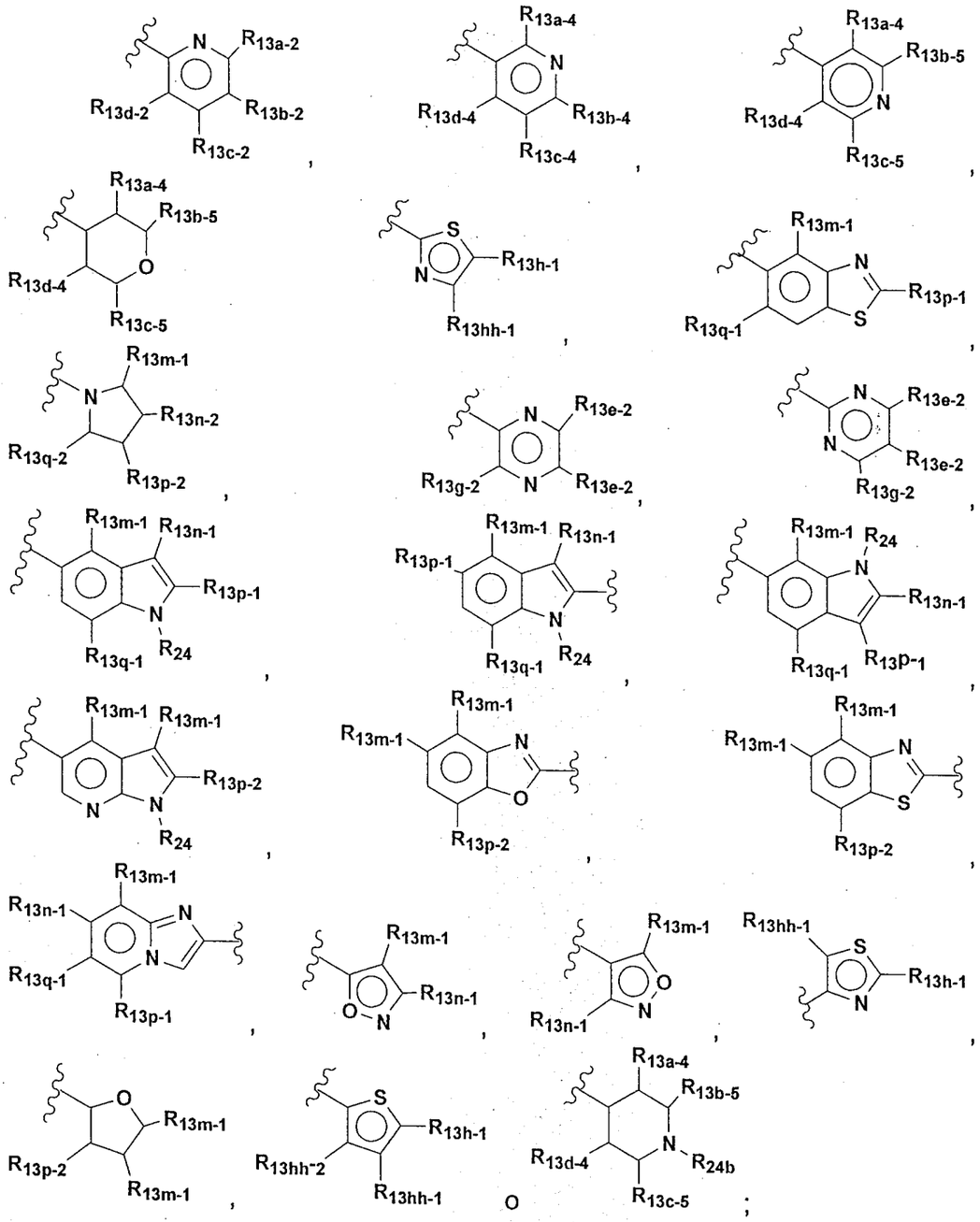





R_1 es ;

R_2 es alquilo C_{1-10}, ciclopropilo opcionalmente sustituido con uno o más R_{13}; cicloalquilo C_{4-10} opcionalmente sustituido con uno o más R_{13bb}; o -$NR_{14}R_{14}$; con la condición de que R_2 no sea -$NR_{14}R_{14}$ cuando m sea 0, 1 ó 3; o

R_2 es ; o

R_2 se selecciona del grupo constituido por:



R_{2a} es alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, $-NR_{14}R_{14}$, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, cualquiera de los cuales está opcionalmente sustituido con uno o más R_{13} y el heteroarilo y

heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{11} y R_{12}, en cada aparición, se seleccionan independientemente de H, alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros y un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

R_{11} y R_{12} se toman junto con el nitrógeno al que están unidos formando un heterociclilo de 4 a 12 miembros, pudiendo estar el heterociclilo opcionalmente sustituido con uno o más R_{13} y el heterociclilo está constituido por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo

están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; con la condición de que cuando R_{13} sea alquilo sustituido con un R_{14a}, R_{14a} no sea -OH;

R_{13a}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13aa}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo

opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2}, en cada aparición, es independientemente H, -OH, F, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos

por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados

independientemente del grupo constituido por N, S u O;

R_{13bb}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

001078

R_{13b-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I,

alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13cc}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo

C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 6 a 12 miembros, un heterociclilo de 6 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, $-NO_2$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, -

$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ o -$CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-4}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ o -$CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-

$NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13dd}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, -

$NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, -

$NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo,

cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13ee}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-1}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con

uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13f}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos

por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos

seleccionados independientemente del grupo constituido por N, S u O;

R_{13h}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13h-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{7-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I,

alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13j}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13m}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12},

alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13m-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13n-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de

4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13p}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13p-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, -

001093

$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ o -$CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13p-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ o -$CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-

$NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, -

$NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{14} se toman junto con los átomos a los que están unidos formando un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-NO_2$, $-CO_2R_{26}$, $-OCONR_{24}R_{24}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-CONR_{24}R_{24}$, $-COR_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$, $-NR_{24}CO_2R_{24}$, $-SO_2NR_{24}R_{24}$, o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{24} se toman junto con los átomos a los que están unidos formando un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-COR_{25}$, $-NR_{25}R_{25}$, $-NR_{25}CO_2R_{25}$, o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24b}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, $-CO_2R_{25}$, $-SO_2NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de

hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O.

3. El compuesto, enantiómero, diastereómero, tautómero o sal del mismo, de la reivindicación 1, en el que:

X es H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Y es H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Z es H, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, cicloalquilo C_{3-10}, un heteroarilo de 6 a 12 miembros, heterociclilo de 4 a 12 miembros, $-NO_2$ o $-NR_{11}R_{12}$;

A es $-(CH_2)_m-R_2$ o $-CH(R_{25})(R_{26})$;

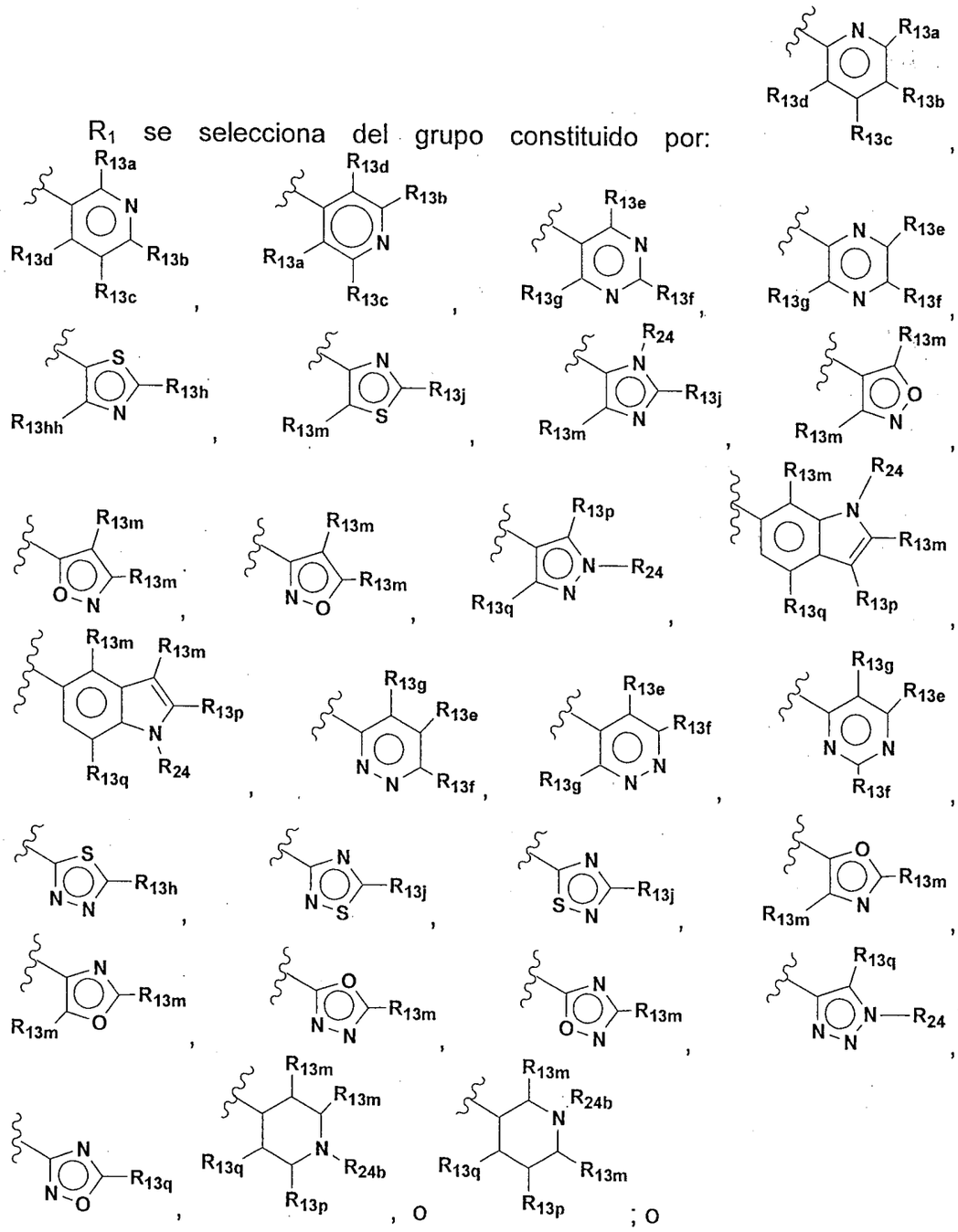
m es 0 a 4;

n es 1 a 4;

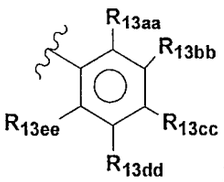
R_1 es F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, alquenilo C_{2-12},

cicloalquilo C_{3-10}, $-(CH_2)_n-SO_2NR_{11}R_{12}$ o $-(CH_2)_n-NR_{11}SO_2R_{12}$, pudiendo estar el alquenilo y cicloalquilo opcionalmente sustituidos con uno o más R_{13}; o

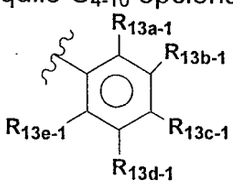
R_1 se selecciona del grupo constituido por:



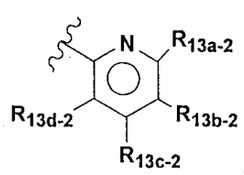
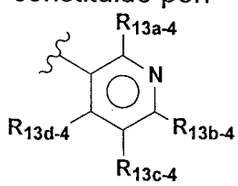
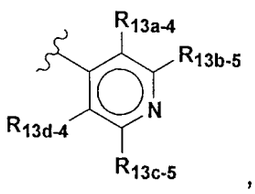
; o

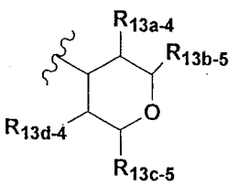
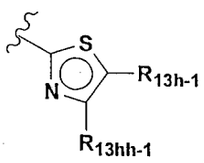
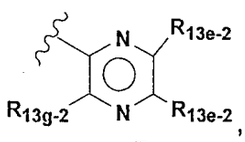
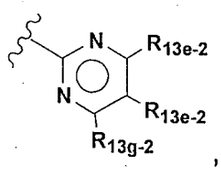
R_1 es  ;

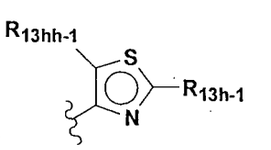
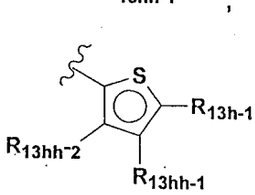
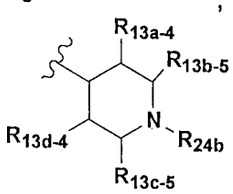
R_2 es alquilo C_{1-10}, ciclopropilo opcionalmente sustituido con uno o más R_{13}; o cicloalquilo C_{4-10} opcionalmente sustituido con uno o más R_{13bb}; o

R_2 es  ; o

R_2 se selecciona del grupo constituido por:

 ,  ,  ,

 ,  ,  ,  ,

 ,  o  ;

R_{11} y R_{12}, en cada aparición, se seleccionan independientemente de H, alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros y un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

001100

R_{11} y R_{12} se toman junto con el nitrógeno al que están unidos formando un heterociclilo de 4 a 12 miembros, pudiendo estar el heterociclilo opcionalmente sustituido con uno o más R_{13} y el heterociclilo está constituido por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ o -$CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; con la condición de que cuando R_{13} sea alquilo sustituido con un R_{14a}, R_{14a} no sea -OH;

R_{13a}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -

001101

$NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13aa}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-1}, en cada aparición, es independientemente -OH, F, Cl, Br, I, alquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, -

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$NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2}, en cada aparición, es independientemente H, -OH, F, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo

estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13bb}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente

sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos

por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos

seleccionados independientemente del grupo constituido por N, S u O;

R_{13c}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$NR_{14}CO_2R_{14}$, -CO_2R_{26}, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ o -$CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13cc}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, -NO_2, -$(CH_2)_m$-SO_2R_{14}, -$NR_{14}SO_2R_{14}$, =O, -$CONR_{14}R_{14}$, -$(CH_2)_m$-$SO_2NR_{14}R_{14}$, -$(CH_2)_m$-$NR_{14}SO_2R_{14}$, -$(CH_2)_n$-$NR_{14}SO_2NR_{14}R_{14}$, -$NR_{14}SO_2NR_{14}R_{14}$, -$CO_2NR_{14}R_{14}$, -$NR_{14}CO_2NR_{14}R_{14}$, -$NR_{14}COR_{14}$, -$SO_2NR_{14}COR_{14}$, -$SO_2NR_{14}CONR_{14}R_{14}$, -$NR_{14}CO_2R_{14}$, -$CO_2R_{14}$, -$NR_{14}R_{14}$, -$NR_{14}CONR_{14}R_{14}$ o -$CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 6 a 12 miembros, un heterociclilo de 6 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, $-NO_2$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-4}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12},

alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de

4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13dd}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, -

$NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-$

$NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13ee}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, -

$NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-1}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, -

$NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13f}, en cada aparición, es independientemente -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo

estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13h}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo

opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13h-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{7-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo

están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13hh-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos

seleccionados independientemente del grupo constituido por N, S u O;

R_{13j}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13m}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13p}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13q}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, alquinilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NO_2$, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, =O, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$ o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14}, en cada aparición, se selecciona independientemente de

hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{14} se toman junto con los átomos a los que están unidos formando un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-NO_2$, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-CONR_{24}R_{24}$, $-COR_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$, $-NR_{24}CO_2R_{24}$, $-SO_2NR_{24}R_{24}$, o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{24} se toman junto con los átomos a los que están unidos formando

un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-NO_2$, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-COR_{25}$, $-NR_{25}CO_2R_{25}$, o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24b}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, $-CO_2R_{25}$, $-SO_2NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos

seleccionados independientemente del grupo constituido por N, S u O.

4. El compuesto, enantiómero, diastereómero, tautómero o sal del mismo, de la reivindicación 1, en el que:

X es H, F, Cl, Br, I, alcoxi C_{1-10}, haloalquilo C_{1-10}, heterociclilo de 4 a 12 miembros, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Y es H, F, Cl, Br, I, alcoxi C_{1-10}, haloalquilo C_{1-10}, heterociclilo de 4 a 12 miembros, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

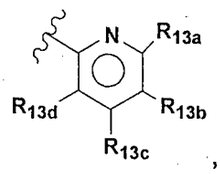
Z es H, Cl, Br, I, alcoxi C_{1-10}, haloalquilo C_{1-10}, heterociclilo de 4 a 12 miembros o $-NR_{11}R_{12}$;

A es $-(CH_2)_m-R_2$;

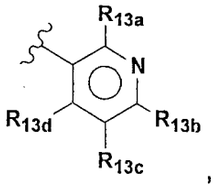
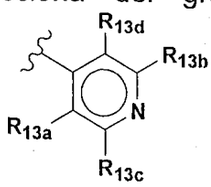
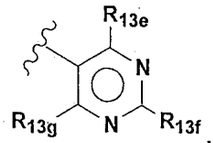
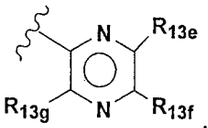
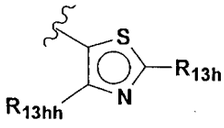
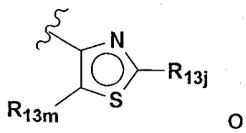
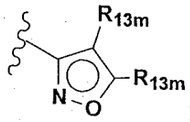
m es 0 a 3;

n es 1 a 3;

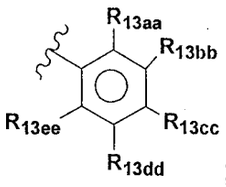
R_1 es Cl, alquenilo C_{2-12}, cicloalquilo C_{3-10}, pudiendo estar el alquenilo y cicloalquilo opcionalmente sustituidos con uno o más R_{13}; o



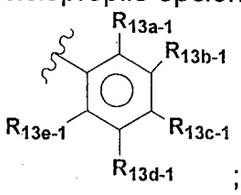
R_1 se selecciona del grupo constituido por:

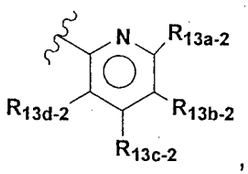
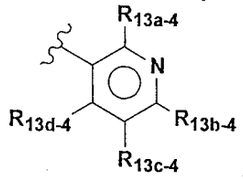
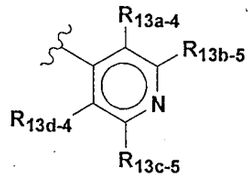
o ; o

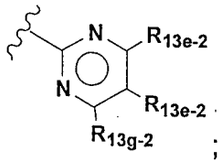
R_1 es  ;

R_2 es ciclopropilo opcionalmente sustituido con uno o más R_{13}; o

R_2 es  ; o

R_2 se selecciona del grupo constituido por:

 ,  ,  o

 ;

R_{11} y R_{12}, en cada aparición, se seleccionan independientemente de H, alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros y un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-$

SO_2R_{14}, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; con la condición de que cuando R_{13} sea alquilo sustituido con un R_{14a}, R_{14a} no sea -OH;

R_{13a}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13aa}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-$

SO_2R_{14}, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, $-NR_{14}CONR_{14}R_{14}$, o $-CONR_{14}OR_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2}, en cada aparición, es independientemente H, -OH, F, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-$

$NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, -

$NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13bb}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o

$-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo

opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos

seleccionados independientemente del grupo constituido por N, S u O;

R_{13cc}, en cada aparición, es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 6 a 12 miembros, un heterociclilo de 6 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12},

arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-4}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-5}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12

miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13dd}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-$

SO_2R_{14}, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-1}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$ o $-CO_2R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$,

$-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-4}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o -

$NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13ee}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-1}, en cada aparición, es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{2-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y

heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13e-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13f}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y

heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13g-2}, en cada aparición, es independientemente H, -OH, F, Cl, Br, I, alquilo C_{2-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó

4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-CONR_{24}R_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

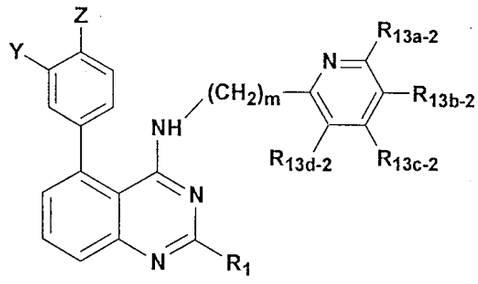
R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4

a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O.

5. El compuesto, enantiómero, diastereómero, tautómero o sal del mismo, de la reivindicación 1, siendo el compuesto un compuesto de fórmula (Ia):

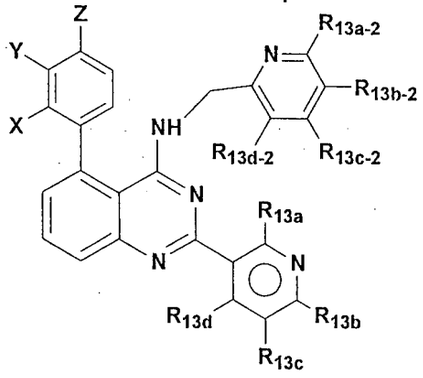


(Ia)

y m, Y, Z, R_1, R_{13a-2}, R_{13b-2}, R_{13c-2} y R_{13d-2} son como se definen en la

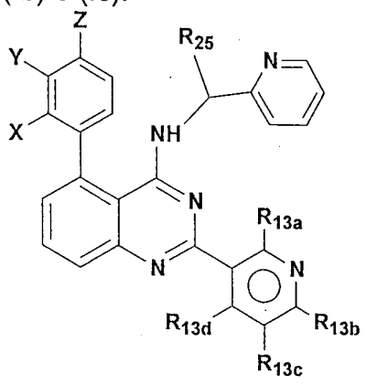
reivindicación 1.

6. Un compuesto de fórmula (Ib) o (Ic):



Ib

o



Ic

o un enantiómero, diastereómero, tautómero o sal del mismo, en las que:

X es H, F, Cl, Br, I, alcoxi C_{1-10}, haloalquilo C_{1-10}, heterociclilo de 4 a 12 miembros, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Y es H, F, Cl, Br, I, alcoxi C_{1-10}, haloalquilo C_{1-10}, heterociclilo de 4 a 12 miembros, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Z es H, Cl, Br, I, alcoxi C_{1-10}, haloalquilo C_{1-10}, heterociclilo de 4 a 12 miembros o $-NR_{11}R_{12}$;

R_{11} y R_{12}, en cada aparición, se seleccionan independientemente de H, alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros y un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2} es independientemente H, -OH, F, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b} es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de

4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-CONR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$ o $-NR_{14}CONR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c} es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, hidroxialquilo C_{1-10}, cianoalquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-(CH_2)_m-SO_2R_{14}$, $-(CH_2)_n-OCONR_{14}R_{14}$, $-NR_{14}SO_2R_{14}$,

$-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$, $-NR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$ o $-NR_{14}CONR_{14}R_{14}$, pudiendo estar el cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, o 3 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, -

$CO_2NR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2} es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-SO_2NR_{14}CONR_{14}R_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo

constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-CO_2H$, $-CO_2R_{26}$, $-OCONR_{24}R_{24}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-CONR_{24}R_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; o

dos R_{24} se toman junto con los átomos a los que están unidos formando un anillo cíclico, pudiendo estar el anillo cíclico opcionalmente sustituido con uno o más R_{24a} y conteniendo opcionalmente 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

con la condición de que X, Y, Z, R_{13a}, R_{13b}, R_{13d}, R_{13a-2}, R_{13b-2}, R_{13c-2} y R_{13d-2} no sean todos H cuando R_{13c} sea $-C(=O)N(C_2H_4OCH_3)_2$, $-SO_2N(C_2H_4OH)_2$.

7. El compuesto, enantiómero, diastereómero, tautómero o sal del mismo, de la reivindicación 6, en la que:

X es H, F, Cl, Br, I, alcoxi C_{1-10}, haloalquilo C_{1-10}, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Y es H, F, Cl, Br, I, alcoxi C_{1-10}, haloalquilo C_{1-10}, $-CO_2R_{11}$ o $-NR_{11}R_{12}$;

Z es H, Cl, Br, I, alcoxi C_{1-10}, haloalquilo C_{1-10} o $-NR_{11}R_{12}$;

R_{11} y R_{12}, en cada aparición, se seleccionan independientemente de H, alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros y un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{13} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del

001146

grupo constituido por N, S u O;

R_{13a} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2} es independientemente H, -OH, F, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b} es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12

miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, o $-NR_{14}CONR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c} es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, hidroxialquilo C_{1-10}, cianoalquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-SO_2NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{26}$, $-NR_{14}R_{14}$, -

$C(=NOR_{14})NR_{14}R_{14}$ o $-NR_{14}CONR_{14}R_{14}$, pudiendo estar el cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2 ó 3 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2} es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó

4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2} es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-CONR_{24}R_{24}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono

y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O.

8. El compuesto, enantiómero, diastereómero, tautómero o sal del mismo, de la reivindicación 6, en el que:

X es H, F, Cl, Br, I, alcoxi C_{1-10} o haloalquilo C_{1-10};

Y es H, F, Cl, Br, I, alcoxi C_{1-10} o haloalquilo C_{1-10};

Z es H, Cl, Br, I, alcoxi C_{1-10} o haloalquilo C_{1-10};

R_{13a} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13a-2} es independientemente H, -OH, F, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

001152

R_{13b} es independientemente H, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CO_2NR_{14}R_{14}$, $-NR_{14}CO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-CO_2R_{14}$, $-NR_{14}R_{14}$, o $-NR_{14}CONR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13b-2} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c} es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, hidroxialquilo C_{1-10}, cianoalquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}COR_{14}$, $-NR_{14}CO_2R_{14}$, $-NR_{14}R_{14}$, $-C(=NOR_{14})NR_{14}R_{14}$ o $-NR_{14}CONR_{14}R_{14}$, pudiendo

estar el cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2 ó 3 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13c-2} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-(CH_2)_n-NR_{14}SO_2NR_{14}R_{14}$, $-NR_{14}SO_2NR_{14}R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d} es independientemente H, -OH, F, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{2-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{13d-2} es independientemente H, -OH, Cl, Br, I, alquilo C_{1-10}, alcoxi C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, alquenilo C_{2-12}, arilo C_{6-10}, un heteroarilo de

4 a 12 miembros, un heterociclilo de 4 a 12 miembros, un heteroaril de 4 a 12 miembros-alquilo C_{1-10}, -CN, $-(CH_2)_m-SO_2R_{14}$, $-NR_{14}SO_2R_{14}$, $-CONR_{14}R_{14}$, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-(CH_2)_m-NR_{14}SO_2R_{14}$, $-CO_2R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el alquilo, cicloalquilo, alquenilo, alcoxi, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14} se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a} se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24} se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo

001155

están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24a} se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25} se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26} se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O.

9. El compuesto, enantiómero, diastereómero, tautómero o sal del mismo, de la reivindicación 6, en el que:

X, Y, Z, R_{13a}, R_{13a-2}, R_{13b-2}, R_{13c-2}, R_{13d} y R_{13d-2} son H;

R_{13b}, en cada aparición, es independientemente H, alcoxi C_{1-10}, o $-NR_{14}R_{14}$;

R_{13c}, en cada aparición, es independientemente H, alquilo C_{1-10},

cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, $-(CH_2)_m-SO_2NR_{14}R_{14}$, $-CONR_{14}R_{14}$ o $-NR_{14}R_{14}$, pudiendo estar el cicloalquilo y heteroarilo opcionalmente sustituidos con uno o más R_{14a} y el heteroarilo está constituido por átomos de carbono y 1, 2 ó 3 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o un heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, cicloalquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con 0-3 R_{14a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{14a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, F, Cl, Br, I, -CN, $-CO_2R_{26}$, $-CO_2NR_{24}R_{24}$, $-OCF_3$, $-OR_{25}$, $-SO_2R_{24}$, $-NR_{24}R_{24}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{24}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, pudiendo estar el alquilo, arilo, heteroarilo y heterociclilo opcionalmente sustituidos con uno o más R_{24a} y el heteroarilo y heterociclilo están constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por

N, S u O;

R_{24a}, en cada aparición, se selecciona independientemente de F, Cl, Br, I, alquilo C_{1-10}, haloalquilo C_{1-10}, arilo C_{6-10}, cicloalquilo C_{3-10}, un heteroarilo de 4 a 12 miembros, un heterociclilo de 4 a 12 miembros, -CN, $-CO_2R_{25}$, $-OCF_3$, $-OR_{25}$, $-CONR_{25}R_{25}$, $-NR_{25}R_{25}$ o aril C_{6-10}-alquilo C_{1-10}, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O;

R_{25}, en cada aparición, se selecciona independientemente de hidrógeno, alquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O; y

R_{26}, en cada aparición, se selecciona independientemente de alquilo C_{1-10}, haloalquilo C_{1-10}, cicloalquilo C_{3-10}, arilo C_{6-10}, un heteroarilo de 4 a 12 miembros o heterociclilo de 4 a 12 miembros, estando el heteroarilo y heterociclilo constituidos por átomos de carbono y 1, 2, 3 ó 4 heteroátomos seleccionados independientemente del grupo constituido por N, S u O.

10. Un compuesto, enantiómero, diastereómero, o sal del mismo, seleccionado de los compuestos expuestos en los ejemplos.

11. Una composición farmacéutica que comprende una cantidad terapéuticamente eficaz de al menos un compuesto de una cualquiera de las reivindicaciones 1 a 10.

12. La composición farmacéutica de la reivindicación 11, que comprende al menos otro agente terapéutico.

13. Un procedimiento para tratar o prevenir arritmia que comprende administrar a un paciente que lo necesite una cantidad eficaz de al menos un compuesto de una cualquiera de las reivindicaciones 1 a 10.

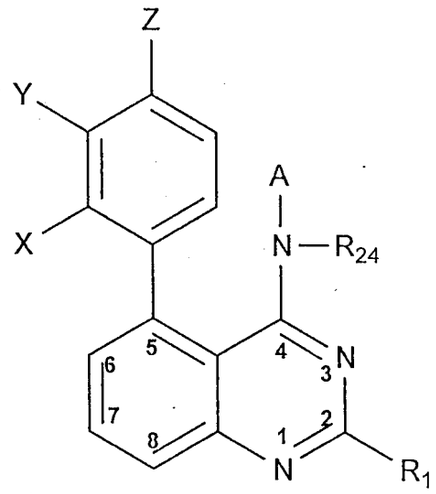
14. Un procedimiento para controlar la frecuencia cardíaca que comprende administrar a un paciente que lo necesite una cantidad eficaz de al menos un compuesto de una cualquiera de las reivindicaciones 1 a 10.

15. Un procedimiento para tratar un estado patológico asociado a I_{Kur} que comprende administrar a un paciente que lo necesite una cantidad eficaz de al menos un compuesto de una cualquiera de las reivindicaciones 1 a 10.

001159

RESUMEN

Un compuesto de fórmula I



en la que A, X, Y, Z, R_1 y R_{24} se describen en el presente documento. Los compuestos son útiles como inhibidores de la función de los canales de potasio y en el tratamiento y prevención de arritmia, trastornos asociados con I_{Kur} y otros trastornos mediados por la función de los canales iónicos.

PODERES

Hayden
1160

TRADUCCIÓN OFICIAL N° 0507071 al español de un documento escrito en inglés, efectuada por Jaime Armando Garavito Burgos, c.c. N° 19.130.702 de Bogotá, Traductor e Intérprete Oficial inglés-español-inglés según Resolución N° 034 de enero 11 de 1983 expedida por el Ministerio de Justicia de la República de Colombia

PODER OTORGADO POR BRISTOL-MYERS SQUIBB COMPANY

APOSTILLA

1. PAÍS: ESTADOS UNIDOS DE AMÉRICA

2. ESTE DOCUMENTO PÚBLICO HA SIDO FIRMADO POR:
SALLY B. HANSEN

3. QUIEN ACTÚA EN CALIDAD DE NOTARIO PÚBLICO DE NUEVA JERSEY

4. LLEVA EL SELLO DE:
SALLY B. HANSEN, NOTARIO

CERTIFICADO

5. EN TRENTON, NUEVA JERSEY

6. EL 28 DE JUNIO DE 2007

7. POR BRADLEY ABELOW, TESORERO DE NUEVA JERSEY

8. N° A295716

9. SELLO (APARECE ADHERIDO SELLO DORADO)

10. FIRMA (FIRMADO) BRADLEY ABELOW

AUTENTICACIÓN DE COPIA DE ORIGINAL
EL SUSCRITO NOTARIO TREINTA Y OCHO(38)(E) CERTIFICA QUE LA PRESENTE COPIA COINCIDE EXACTAMENTE CON EL DOCUMENTO ORIGINAL QUE HE TENIDO A LA VISTA.
07 MAR 2012
NOTARIA 38
RODOLFO RE... MUÑOZ
Notario 38(E) DEL CIRCULO DE BOGOTA D.C.

Texto en inglés y en español mediante el cual **BRISTOL-MYERS SQUIBB COMPANY** domiciliada en Nueva York, Nueva York, otorga poder a **ALVARO CORREA ORDOÑEZ y/o OLGA GEORGETTE OTERO y/o RICARDO METKE y/o JUAN PABLO CONCHA**

Dado y suscrito el 30 de mayo de 2007

(Firmado) Anastasia P. Winslow, Senior Patent Counsel (Abogado de Patentes Senior)

JAIME A. GARAVITO B.
TRADUCTOR E INTERPRETE OFICIAL
RES. 034 DE ENERO 11 DE 1983
MINISTERIO DE JUSTICIA

TRADUCCIÓN OFICIAL N° 0507071 al español de un documento escrito en inglés, efectuada por Jaime Armando Garavito Burgos, c.c. N° 19.130.702 de Bogotá, Traductor e Intérprete Oficial inglés-español-inglés según Resolución N° 034 de enero 11 de 1983 expedida por el Ministerio de Justicia de la República de Colombia

CERTIFICACIÓN NOTARIAL

Texto en inglés y en español mediante el cual el suscrito Notario certifica el 30 de mayo de 2007 la existencia legal de la sociedad **BRISTOL-MYERS SQUIBB COMPANY** así como las funciones y firma de su representante autorizado Anastasia P. Winslow, Senior Patent Counsel (Abogado de Patentes Senior) para lo cual se basó en los documentos relacionados en inglés en el punto 6 de la certificación los cuales se traducen aquí al español, a saber:

Certificación suscrita por el Vicepresidente Senior y el Asesor Legal de Bristol-Myers Squibb Company el 7 de abril de 2007.

Certificado de Constitución Enmendado y Replanteado de Bristol-Myers Squibb Company fechado mayo 24, 2005.

[Firmado] SALLY B. HANSEN, Notario Público

[Sello en tinta que dice: "SALLY B. HANSEN. Notario Público de Nueva Jersey. Mi comisión vence el 6 de junio de 2010"]

[Aparece sello realzado]

AUTENTICACIÓN COPIA DE ORIGINAL
EL SUSCRITO NOTARIO TREINTA Y OCHO DEL CÍRCULO CERTIFICA QUE LA PRESENTE COPIA COINCIDE EXACTAMENTE CON EL DOCUMENTO ORIGINAL QUE HE TENIDO A LA VISTA.
07 MAR 2012
NOTARÍA 38
ADOLFO REY B. ... EZ
NOTARIO DEL CIRCULO DE BOGOTÁ D.C.

La anterior es traducción fiel y completa de la cual se deja copia en esta oficina para su confrontación.

Jaime Armando Garavito Burgos
c.c. N° 19.130.702 de Bogotá
Traductor e Intérprete Oficial según Resolución N° 034 de enero 11 de 1983 expedida por el Ministerio de Justicia

BOGDM5 # 82106

JAIME A. GARAVITO B
TRADUCTOR E INTÉRPRETE OFICIAL
Res. 034 de Enero 11 de 1983
MINISTERIO DE JUSTICIA

APOSTILLE

(CONVENTION DE LA HAYE DU 5 OCTOBRE 1961)

1. COUNTRY: UNITED STATES OF AMERICA

2. THIS PUBLIC DOCUMENT HAS BEEN SIGNED BY:
SALLY B HANSEN

3. ACTING IN THE CAPACITY OF:
NOTARY PUBLIC OF NEW JERSEY

4. BEARS THE SEAL/STAMP OF:
SALLY B HANSEN, NOTARY

CERTIFIED

5. AT TRENTON, NEW JERSEY

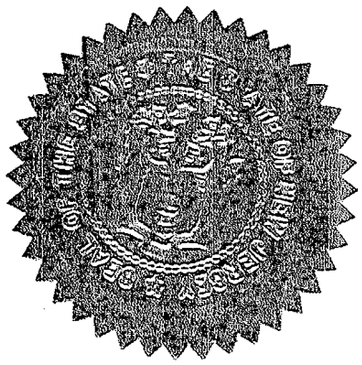
6. THE 28TH DAY OF JUNE 2007

7. BY: Bradley Abelow, NEW JERSEY TREASURER

8. NO. A295716

9. SEAL/STAMP:

10. SIGNATURE



Bradley Abelow



1163

BAKER & MCKENZIE

Raisbeck, Lara, Rodríguez & Rueda
Av. 82 No. 10 - 62 6th Floor
Bogotá, Colombia

NIT: 860.068.840-3
Tel: +57 1 634 1500
Fax: +57 1 376 2211
www.bakernet.com

POWER OF ATTORNEY

The undersigned.

BRISTOL-MYERS SQUIBB COMPANY

domiciled in

Route 206 and Province Line Road, Princeton, New Jersey 08543-4000 United States of America

declares that it hereby grants to

ALVARO CORREA-ORDOÑEZ and/or
OLGA GEORGETTE OTERO and/or
RICARDO METKE and/or
JUAN PABLO CONCHA

with domicile at Av. 82 No. 10 – 62, 6Th floor, of Bogotá D. C., Colombia, a full and sufficient power of attorney to obtain the protection of my (our) industrial property and against the unfair competition, for which purpose I (we) authorize the said attorneys to represent me (us) before any authorities or persons, with or without jurisdiction, specially those administrative, administrative contentious and judicial, as well as before Arbitration Court, in all matters concerning the following: a) Obtainment of patents, utility models, industrial designs, integrated circuits, layout-designs and vegetal varieties; the registration of trademarks, denominations of origin, commercial names, trade emblems, slogans and domain names; its renewal, assignments, change of name or domicile, voluntary cancellation; and the registration of licenses of use of the above rights; b)Processes of protection to the consumer, unfair competition, oppositions, cancellations, nullity, precautionary injunctions, infringement, granting of licenses, writ mandamus, the protection of trade secrets, and in general the civil, penal, an administrative processes relating to those rights. And that in all the above matters they may substitute this Power of Attorney, compromise, conciliate, admit the facts of the case, desist, cancel, receive, resign, and ratify acts done by representatives without a power of attorney.

I hereby ratify all actions previously taken on behalf of this company by the aforementioned attorneys with respect to the mentioned matters.

Done and subscribed in

on the 30 day of May of 2007

Signature of the person issuing the Power

Anastasia P. Winslow
Senior Patent Counsel

PODER DE ABOGADO

La abajo firmada,

BRISTOL-MYERS SQUIBB COMPANY

domiciliada en

Route 206 and Province Line Road, Princeton, New Jersey 08543-4000 Estados Unidos de América

declara por el presente que otorga a

ALVARO CORREA-ORDOÑEZ y/o
OLGA GEORGETTE OTERO y/o
RICARDO METKE y/o
JUAN PABLO CONCHA

con domicilio en la Av. 82 No. 10 – 62 Piso 6 en Bogotá D. C., Colombia, poder especial amplio y suficiente, para obtener la protección de mi (nuestra) propiedad industrial y contra la competencia desleal, a cuyo efecto autorizo (amos) a los dichos apoderados para que me (nos) representen ante cualesquiera autoridades o personas, ejerzan o no jurisdicción, especialmente ante las del orden administrativo, contencioso-administrativo y judicial, así como los tribunales de arbitramento, en todo lo concerniente a los siguientes asuntos: a) Obtención de patentes de invención, modelos de utilidad, diseños industriales, esquemas de trazado de circuitos integrados y variedades vegetales; el registro de marcas, denominaciones de origen, nombres comerciales, enseñas, lemas comerciales y nombres de dominio; su renovación, traspaso, cambio de nombre o domicilio, cancelación voluntaria; y el registro de licencias de uso de esos derechos; b) Los procesos para la protección del consumidor, competencia desleal, oposiciones, cancelaciones, nulidades, medidas cautelares, infracciones, concesión de licencias, la tutela, la protección de secretos industriales, y en general procesos civiles, penales, administrativos relacionados con estos derechos. Y para que en todos los asuntos arriba determinados, puedan sustituir este mandato, transigir, conciliar, admitir los hechos del caso, desistir, cancelar, recibir, renunciar, y ratificar los actos de agentes oficiosos.

Igualmente, ratifico todo lo actuado hasta el momento en los mismos asuntos, por cualquiera de los mencionados apoderados en representación de ésta sociedad.

Dado y firmado en

A los 30 días del mes de mayo de 2007

Firma de la persona que firma el Poder

AUTENTICACION DE COPIA DE ORIGINAL
EL SUSCRITO NOTARIO TREINTA Y OCHO (38) CERTIFICA
QUE LA PRESENTE COPIA COINCIDE EXACTAMENTE CON
EL DOCUMENTO ORIGINAL QUE HE TENIDO A LA VISTA.
07 MAR 2012
NOTARIA 38
RODOLFO REY BERMUDEZ
Notario 38(E) DEL CIRCULO DE BOGOTA D.C.

NOTARIAL CERTIFICATION

On this 30 day of May

2007 , the undersigned Notary

CERTIFIES

That **Name of the person issuing the power**
Anastasia P. Winslow
of legal age and domiciled in
Princeton, NJ USA
Address, city, state, country

set his hand on the foregoing document.

That the grantor is to me personally known and that he/she has legal capacity to execute the instrument.

That the grantor has executed the foregoing document as
Senior Patent Counsel
Position of the person issuing the Power
of the judicial person **BRISTOL-MYERS SQUIBB COMPANY**

That the judicial person **BRISTOL-MYERS SQUIBB COMPANY**

having its home office in

Route 206 and Province Line Road, Princeton, New Jersey 08543-4000 United States of America

is duly organized, has present legal existence and that the purposes for which the power of attorney is granted are within the scope of its corporate purposes.

That the grantor has in fact the referred to authority and that his/her representation is legal.

That I have based certifications 3, 4 and 5 above on the following authentic documents for such purpose exhibited to me and which I mention specifically, giving their dates and their origin or source:
(Please indicate here the documents such as the articles of incorporation, by laws or resolution from the Board of Directors and their dates, on which the notary relied to grant the certification)
- Certification executed by Sr. Vice President and General Counsel of Bristol-Myers Squibb Company on April 7, 2007
- Amended and Restated Certificate of Incorporation of Bristol-Myers Squibb Company dated May 24, 2005

Notary Public
Sally B. Hansen
SALLY B. HANSEN
Notary Public of New Jersey
My Commission Expires June 6, 2010

CERTIFICACION NOTARIAL

A los 30 días del mes de mayo

de 2007 , el suscrito Notario

DA FE

1 Que Anastasia P. Winslow

mayor y domiciliado en Princeton, NJ
Estados Unidos de América

suscribió de su puño y letra el documento que antecede.

2. Que conozco al otorgante y que éste tiene capacidad legal para el otorgamiento.

3 Que el otorgante ha suscrito el referido documento en su carácter de

Abogados de Patentes Senior
de la persona jurídica **BRISTOL-MYERS SQUIBB COMPANY**

4 Que la persona jurídica **BRISTOL-MYERS SQUIBB COMPANY**

con sede en

Route 206 and Province Line Road, Princeton, New Jersey 08543-4000 Estados Unidos de América

está legalmente constituida, que tiene existencia legal actual y que el acto para el cual se otorga el poder está comprendido entre los que constituyen su objeto social.

5 Que el otorgante tiene efectivamente la representación que ostenta y que ésta es legítima.

6. Que he basado las certificaciones 3, 4 y 5 anteriores en los siguientes documentos auténticos que al efecto se me exhibieron y que menciono específicamente con expresión de sus fechas y de su origen o procedencia:
- Certificación suscrita por el Vicepresidente Senior y el Asesor Legal de Bristol-Myers Squibb Company el 7 de abril de 2007.
- Certificado de Constitución Enmendado y Replanteado de Bristol-Myers Squibb Company fechado el 4 de mayo de 2005.

CERTIFICACION DE COPIA DE ORIGINAL
EL SUSCRITO NOTARIO TREINTA Y OCHO(38)(E) CERTIFICA
QUE LA PRESENTE COPIA COINCIDE EXACTAMENTE CON
EL DOCUMENTO ORIGINAL QUE HE TENIDO A LA VISTA.
07 MAR 2012
NOTARIA 38
RODOLFO ALY DE MUDEZ
Notario 38(E) DEL CIRCULO DE BOGOTA D.C.

El Notario Público

CESIÓN DEL INVENTOR
AL SOLICITANTE

VIII-2-1	**Declaration: Entitlement to apply for and be granted a patent** Declaration as to the applicant's entitlement, as at the international filing date, to apply for and be granted a patent (Rules 4.17(ii) and 51bis.1(a)(ii)), in a case where the declaration under Rule 4.17(iv) is not appropriate: Name (LAST, First)	In relation to this international application BRISTOL-MYERS SQUIBB COMPANY is entitled to apply for and be granted a patent by virtue of the following:
VIII-2-1(iv)		an assignment from JOHNSON, James A. to BRISTOL-MYERS SQUIBB COMPANY, dated 14 September 2009 (14.09.2009)
VIII-2-1(iv)		an assignment from LLOYD, John to BRISTOL-MYERS SQUIBB COMPANY, dated 15 September 2009 (15.09.2009)
VIII-2-1(iv)		an assignment from FINLAY, Heather to BRISTOL-MYERS SQUIBB COMPANY, dated 14 September 2009 (14.09.2009)
VIII-2-1(iv)		an assignment from JIANG, Ji to BRISTOL-MYERS SQUIBB COMPANY, dated 14 September 2009 (14.09.2009)
VIII-2-1(iv)		an assignment from NEELS, James to BRISTOL-MYERS SQUIBB COMPANY, dated 17 September 2009 (17.09.2009)
VIII-2-1(iv)		an assignment from DHONDI, Naveen Kumar to BRISTOL-MYERS SQUIBB COMPANY, dated 31 December 2009 (31.12.2009)
VIII-2-1(iv)		an assignment from GUNAGA, Prashantha to BRISTOL-MYERS SQUIBB COMPANY, dated 30 December 2009 (30.12.2009)
VIII-2-1(iv)		an assignment from BANERJEE, Abhisek to BRISTOL-MYERS SQUIBB COMPANY, dated 23 December 2009 (23.12.2009)
VIII-2-1(iv)		an assignment from ADISECHAN, Ashokkumar to BRISTOL-MYERS SQUIBB COMPANY, dated (..)

Industria y Comercio
SUPERINTENDENCIA

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

No. 12-040232- -00000-0000

Fecha: 2012-03-07 16:43:07 Dep: 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 411 PRESENTACION Folios: 1165

PATENTE DE INVENCIÓN ☐ MODELO

- ☐ Indicación que se solicita 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 (De ser el caso formato de descuento)

Completa ☐ Incompleta ☐

PATENTE DE INVENCIÓN PCT ☑ MODELO DE UTILIDAD PCT ☐ Art.33 Decisión 486/00, Circular Única

- ☑ Indicación que se solicita una PCT
- ☑ Copia de la solicitud en español, tal como fue presentada inicialmente (capítulo descriptivo, reivindicatorio, resumen)
- ☑ Dibujos de ser estos pertinentes
- ☑ Comprobante de pago de las tasas establecidas (de ser el caso formato de descuento)

Completa ☑ Incompleta ☐

DISEÑO INDUSTRIAL ☐ (Art. 119 Decisión 486/00)

- ☐ Indicación que se solicita 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 ☐ (Art. 92 Decisión 486/00)

- ☐ Indicación que se solicita un esquema de trazado
- ☐ Datos de identificación del solicitante o de la persona que presenta la solicitud
- ☐ Representación gráfica de un esquema de trazado
- ☐ Comprobante de pago de las tasas establecidas

Completa ☐ Incompleta ☐