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Cuando se reivindiquen varias prioridades, la fecha de la prioridad que se considerará para los propósitos de computar el plazo de 16 meses será la fecha de presentación de la solicitud más antigua cuya prioridad se reivindica.

Formulario PCT/IB/301 (Anexo) (enero de 2004)

From the INTERNATIONAL BUREAU

PCT

SECOND AND SUPPLEMENTARY NOTICE
INFORMING THE APPLICANT OF THE
COMMUNICATION OF THE INTERNATIONAL
APPLICATION (TO DESIGNATED OFFICES
WHICH APPLY THE 30 MONTH TIME
LIMIT UNDER ARTICLE 22(1))

(PCT Rule 47.1(c))

To:

TOFFENETTI, Judith, L.
McDermott, Will & Emery LLP
800 13th Street, N.W.
Washington, DC 20005-3098
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)

03 November 2005 (03.11.2005)

Applicant's or agent's file reference

50183-187

IMPORTANT NOTICE

International application No.

PCT/US2004/020734

International filing date (day/month/year)

29 June 2004 (29.06.2004)

Priority date (day/month/year)

02 July 2003 (02.07.2003)

Applicant

MERCK & CO., INC. et al

1. **ATTENTION:** For any designated Office(s), for which the time limit under Article 22(1), as in force from 1 April 2002 (30 months from the priority date), does not apply, please see Form PCT/IB/308(First Notice) issued previously.

2. Notice is hereby given that the following designated Office(s), for which the time limit under Article 22(1), as in force from 1 April 2002, does apply, has/have requested that the communication of the international application, as provided for in Article 20, be effected under Rule 93bis.1. The International Bureau has effected that communication on the date indicated below:
20 January 2005 (20.01.2005)

AU, AZ, BY, CN, CO, DZ, EP, HU, KG, KP, KR, MD, MK, MZ, NA, RU, SY, TM, US

In accordance with Rule 47.1(c-bis)(i), those Offices will accept the present notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

3. The following designated Offices, for which the time limit under Article 22(1), as in force from 1 April 2002, does apply, have not requested, as at the time of mailing of the present notice, that the communication of the international application be effected under Rule 93bis.1:

AE, AG, AL, AM, AP, AT, BA, BB, BG, BR, BW, BZ, CA, CR, CU, CZ, DE, DK, DM, EA, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KZ, LC, LK, LR, LS, LT, LV, MA, MG, MN, MW, MX, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, SC, SD, SG, SK, SL, TJ, TN, TR, TT, UA, UZ, VC, VN, YU, ZA, ZW

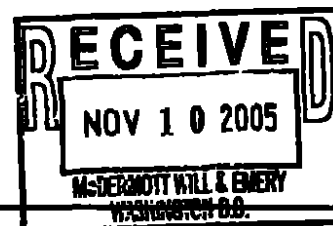
In accordance with Rule 47.1(c-bis)(ii), those Offices accept the present notice as conclusive evidence that the Contracting State for which that Office acts as a designated Office does not require the furnishing, under Article 22, by the applicant of a copy of the international application.

4. TIME LIMITS for entry into the national phase

For the designated or elected Office(s) listed above, the applicable time limit for entering the national phase will, subject to what is said in the following paragraph, be 30 MONTHS from the priority date.

In practice, time limits other than the 30-month time limit will continue to apply, for various periods of time, in respect of certain of the designated or elected Office(s) listed above. For regular updates on the applicable time limits (30 or 31 months, or other time limit), Office by Office, refer to the *PCT Gazette*, the *PCT Newsletter* and the *PCT Applicant's Guide*, Volume II, National Chapters, all available from WIPO's Internet site, at <http://www.wipo.int/pct/en/index.html>.

It is the applicant's sole responsibility to monitor all these time limits.



The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

Nora Lindner

Facsimile No.+41 22 740 14 35

Facsimile No.+41 22 338 89 65

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PCT/US2004/005693

PCT

SEGUNDA NOTIFICACIÓN Y NOTIFICACIÓN SUPLEMENTARIA PARA
INFORMAR AL SOLICITANTE SOBRE LA COMUNICACIÓN DE LA SOLICITUD
INTERNACIONAL (A LAS OFICINAS DESIGNADAS QUE NO APLICAN EL
PLAZO DE 30 MESES CONFORME A LA CLÁUSULA 22(1))

(Norma PCT 47.1(c))

De la OFICINA INTERNACIONAL

Para: TOFFENETTI, Judith L. McDermott, Will & Emery LLP. 600
13th Street, NW. Washington, DC 20005-3096. ESTADOS UNIDOS

Fecha de remisión (día, mes, año): 3 de noviembre de 2005
(3/11/2005)

Referencia de archivo del Solicitante o agente: 50193-187

NOTIFICACIÓN IMPORTANTE

Solicitud Internacional N° PCT/US2004/020734

Fecha de Presentación internacional (día, mes, año): 29 de
junio de 2004 (29-06-2004)

Fecha de Prioridad (día, mes, año): 2 de julio de 2003 (2-07-
2003)

Solicitante: MERCK & CO. LTD. et al

1. ATENCIÓN: Para todas las Oficinas designadas, para las
cuales el plazo conforme a la Cláusula 22(1), vigente desde el

10/6/06
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1 de abril de 2002 (30 meses desde la fecha de la prioridad), sí es aplicable, rogamos ver el Formulario PCT/IB/308 (Primera Notificación) emitido con anterioridad.

2. Por la presente se notifica que las siguientes Oficinas designadas, para las cuales el plazo conforme a la Cláusula 22(1), vigente desde el 1 de abril de 2002, no es aplicable, ha/han solicitado que la comunicación de la solicitud internacional, establecida conforme a la Cláusula 20, se efectuará conforme a la Norma 93bis.1. La Oficina Internacional ha efectuado esa comunicación en la fecha que se indica a continuación:

20 de enero de 2005 (20-01-2005)

AU, AZ, BY, CN, CO, DZ, EP, HU, KG, KP, KR, MD, MK, MZ, NA, RU, SY, TM, US

Conforme a la Norma 47.1(c-bis)(i), esas Oficinas aceptarán la presente Notificación como prueba definitiva de que la comunicación de la solicitud internacional se ha realizado debidamente en la fecha de remisión indicada más arriba y que no es necesario que el solicitante presente copia de la solicitud internacional ante las Oficinas designadas.

2. Las siguientes Oficinas designadas, para las cuales el plazo conforme a la Cláusula 22(1), que está vigente desde el 1 de abril de 2002, no es aplicable, no han solicitado, al

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momento de la remisión de la presente notificación, que la comunicación de la solicitud internacional se efectúe conforme a la Norma 93bis.1:

AE, AG, AL, AM, AP, AT, BA, BB, BG, BR, BW, BZ, CA, CR, CU, CZ, DE, DK, DM, EA, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, ID IL, IN, IS, JP, KE, KZ, LC, LK, LR, LS, LT, LV, MA, MG, MN, MW, MX, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, SC, SD, SG, SK, SL, TJ, TN, TR, TT, UA, UZ, VC, VN, YU, ZA, ZW

Conforme a la Norma 47.1(c-bis)(ii), aquellas Oficinas aceptan la presente notificación como prueba definitiva de que el Estado Firmante por el cual actúa la Oficina como Oficina designada no requiere la provisión, conforme a la Cláusula 22, por el solicitante de una copia de la solicitud internacional.

4. PLAZOS para el ingreso en la fase nacional.

Para las Oficinas designadas o elegidas enumeradas anteriormente, el plazo aplicable para ingresar en la fase nacional será, conforme a lo que se mencionan en el párrafo siguiente, será de 30 MESES desde la fecha de la prioridad.

En la práctica, los plazos excepto el plazo de 30 meses seguirán siendo aplicables, durante diferentes periodos de tiempo, con respecto a ciertas Oficinas designadas o elegidas enumeradas anteriormente. Para actualizaciones regulares de los plazos aplicables (30 o 31 meses, u otro plazo), Oficina

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por Oficina, vea el Boletín del PCT, el Boletín del PCT y la Guía del Solicitante de PCT, Volumen II, Capítulos Nacionales, todos disponibles en el sitio de Internet de la WIPO, en <http://www.wipo.int/pct/en/index.html>.

Es la responsabilidad del solicitante controlar todos estos plazos.

La Oficina Internacional de la WIPO, 34, chemin des Colombettes, 1211 Ginebra 20, Suiza, Fax: (41-22)740.14.35.

Funcionario Autorizado: Nora Lindner

Fax: 41-22-338-8965

Formulario PCT/IB/308 (Segunda Notificación y Notificación Suplementaria) (enero de 2004)

RECEIVED
OCT 14 2004
MW&E
PCT

PATENT COOPERATION TREATY

PCT/US04/020734

From the INTERNATIONAL BUREAU

NOTIFICATION CONCERNING
SUBMISSION OR TRANSMITTAL
OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

To:

TOFFENETTI, Judith, L.
McDermott, Will & Emery LLP
600 13th Street, N.W.
Washington, DC 20005-3098
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 29 September 2004 (29.09.2004)	
Applicant's or agent's file reference 50193-187	IMPORTANT NOTIFICATION
International application No. PCT/US04/020734	International filing date (day/month/year) 29 June 2004 (29.06.2004)
International publication date (day/month/year)	Priority date (day/month/year) 02 July 2003 (02.07.2003)
Applicant MERCK & CO., INC. et al	

- By means of this Form, which replaces any previously issued notification concerning submission or transmittal of priority documents, the applicant is hereby notified of the date of receipt by the International Bureau of the priority document(s) relating to all earlier application(s) whose priority is claimed. Unless otherwise indicated by the letters "NR" in the right-hand column or by an asterisk appearing next to a date of receipt, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- (If applicable) The letters "NR" appearing in the right-hand column denote a priority document which, on the date of mailing of this Form, had not yet been received by the International Bureau under Rule 17.1(a) or (b). Where, under Rule 17.1(a), the priority document must be submitted by the applicant to the receiving Office or the International Bureau, but the applicant fails to submit the priority document within the applicable time limit under that Rule, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- (If applicable) An asterisk (*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b) (the priority document was received after the time limit prescribed in Rule 17.1(a) or the request to prepare and transmit the priority document was submitted to the receiving Office after the applicable time limit under Rule 17.1(b)). Even though the priority document was not furnished in compliance with Rule 17.1(a) or (b), the International Bureau will nevertheless transmit a copy of the document to the designated Offices, for their consideration. In case such a copy is not accepted by the designated Office as the priority document, Rule 17.1(c) provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
02 July 2003 (02.07.2003)	60483,904	US	30 August 2004 (30.08.2004)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 740 14 35	Authorized officer Cruz Juan Facsimile No. +41 22 338 89 65 Telephone No. +41 22 338 8239
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PCT/US2004/020734

TRATADO DE COOPERACIÓN EN MATERIA DE PATENTES

**PCT. NOTIFICACIÓN SOBRE PRESENTACIÓN O REMISIÓN DE DOCUMENTOS
DE PRIORIDAD**

(Instrucciones Administrativas del PCT, Artículo 411)

De la OFICINA INTERNACIONAL

Para: TOFFENETTI

McDermott, Will & Emery LLP

600 13th Street, NW

Washington, DC 20005-3096

Estados Unidos

NOTIFICACIÓN IMPORTANTE

Fecha de envío (día/mes/año): 29 de septiembre de 2004 (29-09-2004)

Referencia de archivo del Solicitante o Agente: 50193-187

Solicitud Internacional No.: PCT/US2004/020734

Fecha de Presentación Internacional: 29 de junio de 2004 (29-06-2004)

Fecha de Publicación Internacional: Aún no publicada

Fecha de Prioridad: 2 de julio de 2003 (2-07-2003)

Solicitante: MERCK & CO., INC. et al

1. Por medio de este Formulario, que reemplaza a toda notificación emitida previamente referida a la presentación o

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remisión de documentos de prioridad, el solicitante por la presente queda notificado de la fecha de recepción del documento de prioridad por la Oficina Internacional en relación con todas las solicitudes anteriores cuya prioridad se reivindica. A menos que se indique lo contrario con las letras "NR", en la columna de la derecha, o con un asterisco que aparece junto a la fecha de recepción, el documento de prioridad referido se presentó o remitió a la Oficina Internacional en cumplimiento de la Norma 17.1(a) o (b).

2. Si corresponde, las letras "NR" que aparecen en la columna de la derecha indican un documento de prioridad que, a la fecha de remisión de este formulario, no había sido recibido aún por la Oficina Internacional conforme a la Norma 17.1(a) o (b). Cuando, conforme a la Norma 17.1(a), el documento de prioridad deba ser presentado por el solicitante ante la Oficina receptora o la Oficina Internacional, pero el solicitante no presente el documento de prioridad dentro del plazo aplicable conforme a esa Norma, se llama la atención del solicitante hacia la Norma 17.1(c) que establece que ninguna Oficina designada podrá pasar por alto la reivindicación de prioridad referida antes de dar al solicitante la oportunidad, al entrar en la fase nacional, de presentar el documento de prioridad dentro de un plazo que sea razonable en las circunstancias.

3. Si corresponde, un asterisco(*) que aparece junto a la fecha de recepción, en la columna de la derecha, indica un documento de prioridad presentado o remitido a la Oficina Internacional pero no en cumplimiento de la Norma 17.1(a) o (b) (el documento de prioridad fue recibido con posterioridad al plazo establecido en la Norma 17.1(a) o el pedido de preparar y remitir el documento de prioridad se presentó ante la Oficina receptora con posterioridad al plazo aplicable conforme a la Norma 17.1(b)). Aún cuando el documento de prioridad no se presentó en cumplimiento con la Norma 17.1(a) o (b), la Oficina Internacional remitirá una copia del documento a las Oficinas designadas, para su consideración. En caso de que esa copia no sea aceptada por la Oficina designada como documento de prioridad, la Norma 17.1(c) establece que ninguna Oficina designada podrá pasar por alto la reivindicación de prioridad referida antes de dar al Solicitante la oportunidad, al entrar en la fase nacional, de presentar el documento de prioridad dentro de un plazo que sea razonable en las circunstancias.

Fecha de la solicitud: 2 de julio de 2003 (2-07-2003)

Solicitud de Prioridad N°: 60/483.904

País u Oficina Regional u Oficina receptora de PCT: Estados Unidos

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Fecha de recepción del documento de prioridad: 30 de agosto de
2004 (30-08-2004)

La Oficina Internacional de la WIPO, 34, chemin des
Colombettes, 1211 Ginebra 20, Suiza. Fax: (41-22) 338.14.35

Funcionario autorizado: Cruz Juan

Teléfono N° (41-22) 338-8965

Fax: (41-22) 338-8239

Formulario PCT/IB/304 (enero de 2004)

From the INTERNATIONAL BUREAU

PCT**NOTIFICATION CONCERNING
TRANSMITTAL OF COPY OF INTERNATIONAL
APPLICATION AS PUBLISHED OR REPUBLISHED**

To:

TOFFENETTI, Judith, L.
McDermott, Will & Emery LLP
600 13th Street, N.W.
Washington, DC 20005-3098
UNITED STATES OF AMERICA

MAY - 5 2005

McDERMOTT WILL & EMERY
WASHINGTON D.C.

IMPORTANT NOTICE

Date of mailing (day/month/year)
28 April 2005 (28.04.2005)Applicant's or agent's file reference
50193-187International application No.
PCT/US2004/020734International filing date (day/month/year)
29 June 2004 (29.06.2004)Priority date (day/month/year)
02 July 2003 (02.07.2003)

Applicant

MERCK & CO., INC. et al

The International Bureau transmits herewith the following documents:

copy of the international application as published by the International Bureau on under
No. WOcopy of international application as republished by the International Bureau on 28 April 2005 (28.04.2005) under
No. WO 2005/005398For an explanation as to the reason for this republication of the international application, reference is made to INID codes (15), (48)
or (88) (as the case may be) on the front page of the attached document.The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.+41 22 740 14 35

Authorized officer

Nora Lindner

Facsimile No.+41 22 338 89 65

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
20 January 2005 (20.01.2005)

PCT

(10) International Publication Number
WO 2005/005398 A3

(51) International Patent Classification: C07D 413/14,
413/10, 487/08, 417/14, A61K 31/422, A61P 31/04

(21) International Application Number:
PCT/US2004/020734

(22) International Filing Date: 29 June 2004 (29.06.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/483,904 2 July 2003 (02.07.2003) US
60/546,984 24 February 2004 (24.02.2004) US

(71) Applicants (for all designated States except US): MERCK
& CO., INC. [US/US]; P.O. Box 2000, Rahway, NJ 07065
(US). KYORIN PHARMACEUTICAL CO., LTD.
[JP/JP]; 5, Kanda Surugadai 2-chome, Chiyoda-ku, Tokyo
(JP).

(72) Inventor: and

(75) Inventor/Applicant (for US only): FUKUDA, Yasunichi
[JP/JP]; 33-2, Utsukusigaoka 3-chome, Oyama, Tochigi
329-0207 (JP).

(74) Agents: TOFFENETTI, Judith, L. et al.; McDermott,
Will & Emery LLP, 600 13th Street, N.W., Washington, DC
20005-3096 (US).

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

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

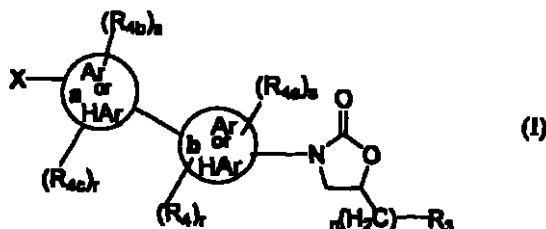
Published:

- with international search report
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(88) Date of publication of the international search report:
28 April 2005

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

(54) Title: CYCLOPROPYL GROUP SUBSTITUTED OXAZOLIDINONE ANTIBIOTICS AND DERIVATIVES THEREOF



(57) Abstract: This invention relates to new oxazolidinones having a cyclopropyl moiety, which are effective against aerobic and
anerobic pathogens such as multi-resistant staphylococci, streptococci and enterococci, Bacteroides spp., Clostridia spp. species, as
well as acid-fast organisms such as Mycobacterium tuberculosis and other mycobacterial species. The compounds are represented
by structural formula: (I): its enantiomer, diastereomer, or pharmaceutically acceptable salt or ester thereof.

WO 2005/005398 A3

INTERNATIONAL SEARCH REPORT

Application No
PCT/US2004/020734

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D413/14 C07D413/10 C07D487/08 C07D417/14 A61K31/422
A61P31/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	US 2004/147760 A1 (THOMAS RICHARD CHARLES 'US' ET AL) 29 July 2004 (2004-07-29) examples 48-51, 54-57, 65, 72, 73 claim 70	1, 2, 7, 8, 10-15
P.X	WO 2004/048350 A (ASTRAZENECA AB; ASTRAZENECA UK LIMITED; GRAVESTOCK, MICHAEL, BARRY; HA) 10 June 2004 (2004-06-10) page 78, line 24 - page 79; claim 1 example 8	1, 2, 7, 8, 10-15

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *A* document member of the same patent family

Date of the actual completion of the international search

9 February 2005

Date of mailing of the international search report

21 02 05

Name and mailing address of the ISA

European Patent Office, P.O. 5818 Patentplan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+31-70) 340-3018

Authorized officer

Kollmannsberger, M

INTERNATIONAL SEARCH REPORT

Application No
PCT/US2004/020734

102718

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/94342 A (DONG A PHARM CO LTD ; CHO JONG HWAN (KR); CHOI SUNG HAK (KR); LEE JAE) 13 December 2001 (2001-12-13) cited in the application claims examples 42, 78, 119, 129, 132, 134, 136, 139, 143, 146, 148	1, 2, 7, 8, 10-15 ~~1028~~
X	US 5 523 403 A (BARBACHYN ET AL) 4 June 1996 (1996-06-04) claim 1 column 46, line 1 - line 3 column 46, line 10 - line 12	1, 2, 7, 8, 10-15
X	WO 94/13649 A (THE UPJOHN COMPANY; BARBACHYN, MICHAEL, ROBERT) 23 June 1994 (1994-06-23) claim 1 page 64, line 20 - line 21 page 64, line 26 - line 27	1, 2, 7, 8, 10-15
A	WO 03/027083 A (KYORIN SEIYAKU KK ; FUKUDA YASUMICHI (JP); MERCK & CO INC (US); HANMON) 3 April 2003 (2003-04-03) claims	1-15
A	EP 0 352 781 A (E.I. DU PONT DE NEMOURS AND COMPANY) 31 January 1990 (1990-01-31) cited in the application example 38	1, 2, 7, 8, 10-15
A	US 5 736 545 A (GADWOOD ET AL) 7 April 1998 (1998-04-07) column 1, line 43 - column 2, line 14	1, 2, 7, 8, 10-15

oral application No.
PCT/US2004/020734

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

- Box III Observations where unity of invention is lacking (Continuation of Item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Flammark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1,2, 4-6,10-15 (all in part), 3,9

compounds according to structure (I) of claim 1 in which X
is a bicyclo[3.1.0]-ring and their uses

2. claims: 1,2,4-6,10-15 (all in part); 7,8

compounds according to structure (I) of claim 1 in which X
is an N-bound heterocycle

INTERNATIONAL SEARCH REPORT

Info Application No
PCT/US2004/020734

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Publication No
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Int. Application No
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TRATADO DE COOPERACIÓN EN MATERIA DE PATENTES**PCT****NOTIFICACIÓN REFERIDA A LA REMISIÓN DE COPIA DE SOLICITUD DE
PATENTE INTERNACIONAL PUBLICADA O REPUBLICADA****De la OFICINA INTERNACIONAL****Para: TOFFENETTI, Judith L. McDermott, Will & Emery LLP. 600
13th Street, NW. Washington, DC 20005-3096. ESTADOS UNIDOS****Fecha de remisión (día/mes/año): 28 de abril de 2004 (28-04-
2004)****Referencia de archivo del Solicitante o del agente: 50193-187****NOTIFICACIÓN IMPORTANTE****Solicitud Internacional N° PCT/US2004/020734****Fecha de Presentación internacional (día/mes/año): 29 de junio
de 2004 (29-06-2004)****Fecha de la Prioridad (día/mes/año): 2 de julio de 2003 (2-07-
2003)****Solicitante: MERCK & CO., INC et al****La Oficina Internacional remite adjunto a la presente los
siguientes documentos:****[] Copia de la solicitud de patente internacional publicada
por la Oficina Internacional el con el N° WO**680
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[X] copia de la solicitud de patente internacional republicada por la Oficina Internacional el 28 de abril de 2005 con el N° WO 2005/005398

Para ver una explicación en cuanto al motivo de esta republicación de la solicitud internacional, se hace referencia a los códigos de INID (15), (48) u (88) (según sea el caso) que aparecen en la carátula del documento adjunto a la presente.

La Oficina Internacional de la WIPO

34, chemin des Colombettes, 1211 Geneva 20, Suiza

Fax 41-22-740-1435

Funcionario Autorizado: Nora Lindner. Fax 41-22-338-8965

Formulario PCT/IB/311 (enero de 2004)

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p358

(12) SOLICITUD INTERNACIONAL PUBLICADA DE ACUERDO CON EL
TRATADO DE COOPERACIÓN EN MATERIA DE PATENTES (PCT)

(19) ORGANIZACIÓN MUNDIAL DE LA PROPIEDAD INTELECTUAL

Oficina Internacional

WIPO - OMPI

PCT

(43) Fecha de Publicación Internacional: 20 de enero de 2005

(20-01-2005)

(10) Publicación Internacional Número: WO 2005/005398 A3

(51) Clasificación Internacional de Patentes⁷: C07D 413/14,
413/10, 487/08, 417/14, A61K 31/422, A61P 31/04

(21) Solicitud Internacional Número: PCT/US2004/020734

(22) Fecha de Presentación Internacional: 29 de junio de 2004

(29-06-2004)

(25) Idioma de Presentación: inglés

(26) Idioma de Publicación: inglés

(30) Datos de la Prioridad:

60/483.904 2 de julio de 2003 (2-07-2003) US

60/546.984 24 de febrero de 2004 (24-02-2004) US

(71) Solicitante (para todos los Estados designados excepto Estados Unidos): MERCK & CO. INC. (US/US), P.O. Box 2000, Rahway, NJ 07065 (Estados Unidos). KYORIN PHARMACEUTICAL CO., LTD. [JP/JP], 5, Kanda Surugadai 2-chome, Chiyoda-ku, Tokio (Japón).

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(72) Inventores; y

(75) Inventores/Solicitantes (exclusivamente para Estados Unidos): FUKUDA, Yasumichi [Japón/Japón], 33-2, Utsukusigoaka 3-chome, Oyama, Tochigi 329-0207 (Japón).

(74) Agentes: TOFFENETTI, Judith L. et al, McDermott, Will & Emery LLP, 600 13th Street, NW, Washington, DC 20005-3096 (Estados Unidos).

(81) Estados Designados (excepto que se indique de otro modo para todos los tipos de protecciones nacionales existentes):
AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Estados Designados (salvo que se indique de otro modo, para todos los tipos de protecciones regionales existentes):
Patente ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Patente de Eurasia (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), Patente Europea (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), Patente OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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también organismos ácidos rápidos como *Mycobacterium tuberculosis* y otras especies micobacterianas. Los compuestos están representadas por la fórmula estructural: (I): su enantiómero, diastereómero o sal farmacéuticamente aceptable, o éster de los mismos.

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INFORME DE BÚSQUEDA INTERNACIONAL

Solicitud Internacional No. PCT/US2004/020734

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A. Clasificación de la Materia:

IPC 7: C07D413/14 C07D413/10 C07D487/08 C07D417/14 A61K31/422
A61P31/04

De acuerdo con la Clasificación Internacional de Patentes
(IPC) o con la clasificación nacional e IPC.

B. Campos de Búsqueda:

Documentación mínima buscada (sistema de clasificación seguido
por símbolos de clasificación)

IPC 7 C07D A61K A61P

Documentación buscada además de la documentación mínima en la
medida en que tales documentos están incluidos en los campos
de búsqueda:

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Base de datos electrónica consultada durante la búsqueda
internacional (nombre de la base de datos y, si es posible,
términos de búsqueda usados):

EPO-Internal, WPI Data, CHEM ABS Data

C. Documentos Considerados Relevantes

Categoría*	Cita de documento, indicando, si corresponde, los pasajes relevantes	Relevante para la reivindicación N°
E	US 2004/147760 A1 (THOMAS RICHARD CHARLES US ET AL) 29 de julio de 2004 (29-07-2004) Ejemplos 48-51, 54-57, 65, 72, 73 Reivindicación 70	1, 2, 17, 8, 10-15
P, X	WO 2004/048350 (ASTRAZENECA AB; ASTRAZENEKA UK LIMITED; GRAVESTOCK MICHAEL, BARRY; HA) 10 de junio de 2004 (10-06-2004) página 78, línea 24 - página 79; reivindicación 1, ejemplo 8	1, 2, 7, 8, 10-15

[x] Se mencionan otros documentos en la continuación del
Casillero C.

[x] Se mencionan miembros de familia de patente en el anexo.

*** Categorías especiales de documentos citados:**

"A": documento que define el estado general del arte que no se considera de particular relevancia

"E": documento anterior pero publicado en la fecha de presentación internacional o con posterioridad a ella.

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"L": documento que puede arrojar dudas sobre la reivindicación de prioridad o que se cita para establecer la fecha de publicación de otra cita o por otra razón especial (especificada).

"O": documento que refiere a una revelación oral, uso, exhibición u otro medio.

"P": documento publicado antes de la fecha de presentación internacional pero con posterioridad a la fecha de prioridad reivindicada.

"T": documento posterior publicado con posterioridad a la fecha de presentación internacional o a la fecha de prioridad y que no está en conflicto con la solicitud pero citado para comprender un principio o teoría que sustenta la invención.

"X": documento de particular relevancia: la invención reivindicada no puede considerarse nueva o no puede considerarse que implica un paso inventivo cuando el documento se toma solo.

"Y": documento de particular relevancia: la invención reivindicada no puede considerarse que implica un paso inventivo cuando el documento se combina con otro u otros documentos, siendo dicha combinación obvia para un experto en el arte.

"&": documento miembro de la misma familia de patentes.

Fecha de la finalización efectiva de la búsqueda internacional: 9 de febrero de 2005

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Fecha de envío del informe de búsqueda internacional: 21-02-05

Nombre y domicilio para correspondencia de la ISA

Oficina de Patentes Europea, P.B. 5818 Patentlaan 2

NL-2280 HV Rijswijk

Tel: (31-70) 340-2040. Tx 31 651 epo nl

Fax: (31-70) 340-3016

Funcionario autorizado: Kollmannsberger, M

Formulario PCT/ISA/210 (página dos) (enero de 2004)

INFORME DE BÚSQUEDA INTERNACIONAL

Solicitud internacional N°: PCT/US2004/020734

C. (Continuación) Documentos Considerados Relevantes

Categoría*	Cita de documento, indicando, si corresponde, los pasajes relevantes	Relevante para la reivindicación N°
X	WO 01/94342 A (DONG A PHARM CO LTD, CHO JONG HWAN (KR); CHOI SUNG HAK (KR); LEE JAE) 13 de diciembre de 2001 (13-12-2001) citada en la solicitud Reivindicaciones Ejemplos 42, 78, 119, 129, 132, 134, 136, 139, 143, 146, 148	1, 2, 7, 8, 10-15
X	US 5.523.403 A (BARBACHYN ET	1, 2, 7, 8, 10-15

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	AL) 4 de junio de 1996 (4-06-1996) reivindicación 1 Columna 46, línea 1 - línea 3 Columna 46, línea 10 - línea 12	
X	WO 94/13649 A (THE UPJOHN COMPANY; BARBACHYN, MICHAEL, ROBERT) 23 de junio de 1994 (23-06-1994) reivindicación 1 Página 64, línea 20 - línea 21 Página 64, línea 26 - línea 27	1, 2, 7, 8, 10-15
A	WO 03/027083 A (KYORIN SEIYAKU KK; FUKUDA YASUMICHI (JP) MERCK & CO INC (US); HAMMON) 3 de abril de 2003 (3-04-2003) Reivindicaciones	1-15
A	EP 0.352.781 A (E.I. DU PONT DE MEMOURS AND COMPANY) 31 de enero de 1990 (31-01-1990) citada en la solicitud Ejemplo 38	1, 2, 7, 8, 10-15
A	US 5.736.545 A (GADWOOD ET AL) 7 de abril de 1998 (7-04-1998) columna 1, línea 43 - columna 2, línea 14	1, 2, 7, 8, 10-15

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INFORME DE BÚSQUEDA INTERNACIONAL

Solicitud Internacional N° PCT/US2004/020734

Casillero N° II. Observaciones cuando ciertas reivindicaciones se consideraron no buscables (Continuación del punto 2 de la página 1).

Este Informe de Búsqueda Internacional no se ha establecido con respecto a ciertas reivindicaciones conforme a la Cláusula 17(2)(a) por los siguientes motivos:

1. ☒ Reivindicaciones N°:

porque se relacionan con un objeto que no se requiere que busque esta Autoridad, a saber:

Aunque las reivindicaciones 14 y 15 se refieren a un método de tratamiento del cuerpo humano/animal, la búsqueda se ha realizado y basado en los supuestos efectos del compuesto/composición.

2. ☐ Reivindicaciones N°:

porque se relacionan con partes de la solicitud internacional que no cumplen con los requisitos establecidos en tal magnitud que no se puede realizar una búsqueda significativa, específicamente:

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3. ☐ Reivindicaciones N°:

porque son reivindicaciones dependientes y no están redactadas de acuerdo con la segunda y tercera oraciones de la Norma 6.4(a).

Casillero N° III. Observaciones cuando falta unidad de invención (Continuación del punto 3 de la página 1)

La Autoridad de Búsqueda Internacional encontró varias invenciones en esta solicitud internacional, a saber:

Véase la página adicional

1. ☒ Como todos los aranceles de búsqueda adicionales se pagaron oportunamente por el solicitante, este informe de búsqueda internacional abarca todas las reivindicaciones buscables.

2. ☐ Como las reivindicaciones buscables pudieron buscarse sin esfuerzo que justifique un arancel adicional, esta Autoridad no intima al pago de ningún arancel adicional.

3. ☐ Como ninguno de los aranceles de búsqueda adicionales requeridos se pagaron oportunamente por el solicitante, este informe de búsqueda internacional abarca solamente aquellas reivindicaciones para las cuales se pagaron aranceles, específicamente las reivindicaciones N°:

4. ☐ El solicitante no pagó ninguno de los aranceles de búsqueda adicionales. En consecuencia, este informe de

búsqueda internacional se limita a la invención mencionada en primer lugar en las reivindicaciones; está abarcada por las reivindicaciones N°:

Observación Bajo Protesta:

☐ Los aranceles de búsqueda adicionales estuvieron acompañados por el protesto del solicitante

☒ Ningún protesto acompañó el pago de los aranceles de búsqueda adicionales.

Formulario PCT/ISA/210 (continuación de la página 1 (2))
(enero de 2004)

Solicitud Internacional N° PCT/US2004/020734

OTRA INFORMACIÓN CONTINUACIÓN DE PCT/ISA/210

Esta Autoridad de Búsqueda Internacional encontró varias (grupos de) invenciones en esta solicitud internacional, a saber:

1. reivindicaciones: 1, 2, 4-6, 10-15 (todas en parte), 3, 9
compuestos de acuerdo con la estructura (I) de la reivindicación 1 en donde X es un anillo de biciclo'3.1.0 y sus usos

2. reivindicaciones: 1, 2, 4-6, 10-15 (todas en parte); 7, 8
compuestos de acuerdo con la estructura (I) de la reivindicación 1 en donde X es heterociclo unido a N.

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INFORME DE BÚSQUEDA INTERNACIONAL

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Información sobre miembros de familia de patentes

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Información sobre miembros de familia de patentes

Solicitud Internacional N° PCT/US2004/020734

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6/9/04

INFORME DE BÚSQUEDA INTERNACIONAL

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Información sobre miembros de familia de patentes

Solicitud Internacional N° PCT/US2004/020734

Documento patente citado en informe búsqueda	Fecha de publicación	Miembro(s) de familia de patentes	Fecha de publicación
US 5736545	A	NZ 331011 A	28-04-2000
		PT 883611 T	31-12-2002
		SI 883611 T1	31-12-2002
		TW 442460 B	23-06-2001
		WO 9730981 A1	28-08-1997
		ZA 9701287 A	14-08-1998

From the INTERNATIONAL BUREAU

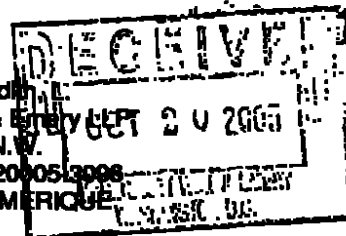
PCT

INFORMATION CONCERNING ELECTED OFFICES NOTIFIED OF THEIR ELECTION

(PCT Article 31(7) and Rule 61.3)

To:

TOFFENETTI, Judith
McDermott, Will & Emery
600 13th Street, N.W.
Washington, DC 20005-3006
ETATS-UNIS D'AMERIQUE



Date of mailing (day/month/year) 13 October 2005 (13.10.2005)		
Applicant's or agent's file reference 50193-187		IMPORTANT INFORMATION
International application No. PCT/US2004/020734	International filing date (day/month/year) 29 June 2004 (29.06.2004)	
Priority date (day/month/year) 02 July 2003 (02.07.2003)		
Applicant MERCK & CO., INC. et al		

- The applicant is hereby informed that the International Bureau has, according to Article 31(7), notified each of the following Offices of its election:
EP: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR
National: BG, CA, CN, CZ, DE, JP, KP, KR, MN, NO, PL, RO, RU, SK, US
- The following Offices have waived the requirement for the notification of their election; the notification will be sent to them by the International Bureau only upon their request:
AP: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW
EA: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
OA: BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
National: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BR, BW, BY, BZ, CH, CO, CR, CU, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MW, MX, MZ, NA, NI, NZ, OM, PG, PH, PT, SC, SD, SE, SG, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
- Since the election(s) was (were) made after the expiration of 19 months from the priority date, the applicant is reminded that he must, subject to the following paragraph, enter the national phase within 20 months from the priority date (or later in some Offices) before some of the designated Offices in respect of which Article 22(1), as modified with effect of 1 April 2002, does not apply, by paying the national fee(s) and furnishing, if prescribed, a translation of the international application.

 However, in respect of most other designated Offices, the time limit of 30 months (or later) may nevertheless apply. See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, use the *PCT Applicant's Guide*, Volume II, National Chapters, the *PCT Newsletter* and the WIPO Internet site, updated regularly.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Nora Lindner
Facsimile No.+41 22 740 14 35	Facsimile No.+41 22 338 89 65

TRATADO DE COOPERACIÓN EN MATERIA DE PATENTES

PCT

INFORMACIÓN CONCERNIENTE A LAS OFICINAS ELEGIDAS NOTIFICADAS
DE SU ELECCIÓN

(PCT, Cláusula 31(7) y Norma 61.3)

De: Oficina Internacional

Para: TOFFENETTI, Judith L. McDermott, Will & Emery LLP. 600
13th Street, NW. Washington, DC 20005-3096. Estados Unidos

NOTIFICACIÓN IMPORTANTE

Fecha de remisión (día/mes/año): 13 de octubre de 2005 (13-10-
2005)

Referencia de archivo de Solicitante o agente: 50193-187

Solicitud Internacional No: PCT/US2004/020734

Fecha de Presentación Internacional: 29 de junio de 2004 (29-
06-2004)

Fecha de prioridad: 2 de julio de 2003 (2-07-2003)

Solicitante: MERCK & CO. INC. et al

1. Por la presente se informa al solicitante que la Oficina
Internacional ha notificado, conforme a la Cláusula 31(7), a
cada una de las siguientes Oficinas de su elección:

EP: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
NL, PT, RO, SE, SI, SK, TR

Nacional: BG, CA, CN, CZ, DE, JP, KP, KR, MN, NO, PL, RO, RU, SK, US

2. Las siguientes Oficinas han renunciado al requisito de notificación de su elección; la notificación les será remitida por la Oficina Internacional sólo a su pedido:

AP: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW

EA: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

OA: BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

Nacional: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BR, BW, BY, BZ, CH, CO, CR, CU, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IN, IS, KE, KG, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MW, MX, MZ, NA, NI, NZ, OM, PG, PH, PT, SC, SD, SE, SG, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

3. Dado que la elección(es) se hizo (hicieron) con posterioridad al vencimiento de 19 meses desde la fecha de prioridad, se recuerda al solicitante que debe, conforme al siguiente párrafo, ingresar en la fase nacional dentro de los 20 meses desde la fecha de prioridad (o con posterioridad en algunas Oficinas) ante algunas de las oficinas designadas con respecto a las cuales la Cláusula 22(1) y sus modificaciones con vigencia el 1 de abril de 2002, no es aplicable, pagando el arancel(es) nacional y proporcionando, si está establecido, una traducción de la solicitud internacional.

Sin embargo, con respecto a la mayor parte de las demás Oficinas, el plazo de 30 meses (o posterior) puede de todos modos ser aplicable. Véase el Anexo al Formulario PCT/IB/301 y, para detalles acerca de los plazos aplicables, Oficina por

Oficina, véase la Guía del Solicitante por PCT, Volumen II, Capítulos Nacionales, el Boletín del PCT y el sitio de Internet de la OMPI, actualizado regularmente.

La Oficina Internacional de WIPO, 34, chemin des Colombettes, 1211 Ginebra 20, Suiza. Fax: (41-22)740 1435

Firma autorizada: Nora Lindner. Fax: 41-22-338-8965

Formulario PCT/IB/332 (enero de 2004)

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The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line below:

IPEA/EP

PCT

CHAPTER II

DEMAND

under Article 31 of the Patent Cooperation Treaty:
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty.

For International Preliminary Examining Authority use only			
Identification of IPEA		Date of receipt of DEMAND	
Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION		Applicant's or agent's file reference 50193-187	
International application No. PCT/US2004/020734	International filing date (day/month/year) 29 June 2004 (29/06/04)	(Earliest) Priority date (day/month/year) 02 July 2003 (02/0703)	
Title of invention CYCLOPROPYL GROUP SUBSTITUTED OXAZOLIDINONE ANTIBODIES AND DERIVATIVES THEREOF			
Box No. II APPLICANT(S)			
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of) MERCK & CO., INC. P.O. Box 2000 Rahway, NJ 07065 US		Telephone No.	
		Facsimile No.	
		Teleprinter No.	
		Applicant's registration No. with the Office	
State (that is, country) of nationality: US		State (that is, country) of residence: US	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) KYORIN PHARMACEUTICALS CO., LTD. 5, Kanda Surugadai 2-chome Chiyoda-ku, Tokyo JP			
State (that is, country) of nationality: JP		State (that is, country) of residence: JP	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) FUKUDA, Yasumichi 33-2, Utsukusigaoka 2-chome Oyama, Tochigi 328-0207 JP			
State (that is, country) of nationality:		State (that is, country) of residence:	
☐ Further applicants are indicated on a continuation sheet.			

Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The following person is ☒ agent ☐ common representative
 and ☒ has been appointed earlier and represents the applicant(s) also for international preliminary examination.
☐ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.
☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.

Name and address: (Family name followed by given names; for a legal entity, full official designation. The address must include postal code and name of country.)

TOFFENETTI, Judith L.
 McDERMOTT WILL & EMERY LLP
 600 13th Street, NW
 Washington, DC 20005-2066
 US

Telephone No.

202-756-8000

Facsimile No.

202-756-8087

Teleprinter No.

Agent's registration No. with the Office

39,048

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION**Statement concerning amendments:***

1. The applicant wishes the international preliminary examination to start on the basis of:

☒ the international application as originally filed

the description ☐ as originally filed

☒ as amended under Article 34

the claims ☐ as originally filed

☐ as amended under Article 19 (together with any accompanying statement)

☒ as amended under Article 34

the drawings ☐ as originally filed

☐ as amended under Article 34

2. ☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.

3. ☒ Where the IPEA wishes to start the international preliminary examination at the same time as the international search in accordance with Rule 69.1(b), the applicant requests the IPEA to postpone the start of the international preliminary examination until the expiration of the applicable time limit under Rule 69.1(d).

4. ☐ The applicant expressly wishes the international preliminary examination to start earlier than at the expiration of the applicable time limit under Rule 54bis.1(a).

* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: **English**

☒ which is the language in which the international application was filed.

☐ which is the language of a translation furnished for the purposes of international search.

☐ which is the language of publication of the international application.

☐ which is the language of the translation (to be) furnished for the purposes of international preliminary examination.

Box No. V ELECTION OF STATES

The filing of this demand constitutes the election of all Contracting States which are designated and are bound by Chapter II of the PCT.

Box No. VI CHECK LIST

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:

- | | | |
|--|---|-----------|
| 1. translation of international application | : | sheets |
| 2. amendments under Article 34 | : | 41 sheets |
| 3. copy (or, where required, translation) of amendments under Article 19 | : | sheets |
| 4. copy (or, where required, translation) of statement under Article 19 | : | sheets |
| 5. letter | : | sheets |
| 6. other (specify) | : | sheets |

For International Preliminary Examining Authority use only

received	not received
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐

The demand is also accompanied by the item(s) marked below:

- | | |
|--|---|
| 1. ☒ fee calculation sheet | 5. ☐ statement explaining lack of signature |
| 2. ☐ original separate power of attorney | 6. ☐ sequence listing in electronic form |
| 3. ☐ original general power of attorney | 7. ☐ tables in electronic form related to a sequence listing |
| 4. ☐ copy of general power of attorney; reference number, if any: | 8. ☐ other (specify): |

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).


Juan L. TOFFENETTI

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:

2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):

- | | |
|--|--|
| 3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply.
☐ The applicant has been informed accordingly. | 6. ☐ The date of receipt of the demand is AFTER the expiration of the time limit under Rule 54bis.1(a) and item 7 or 8, below, does not apply. |
| 4. ☐ The date of receipt of the demand is WITHIN the time limit of 19 months from the priority date as extended by virtue of Rule 80.5. | 7. ☐ The date of receipt of the demand is WITHIN the time limit under Rule 54bis.1(a) as extended by virtue of Rule 80.5. |
| 5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82. | 8. ☐ Although the date of receipt of the demand is after the expiration of the time limit under Rule 54bis.1(a), the delay in arrival is EXCUSED pursuant to Rule 82. |

For International Bureau use only

Demand received from IPEA on:

1057 200

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FEE CALCULATION SHEET

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Annex to the Demand

International application No. PCT/US2004/020734		For International Preliminary Examining Authority use only	
Applicant's or agent's file reference 60193-187		Date stamp of the IPEA	
Applicant MERCK & CO., INC.			
CALCULATION OF PRESCRIBED FEES			
1. Preliminary examination fee		1,630.00	P
2. Handling fee (<i>Applicants from certain States are entitled to a reduction of 75% of the handling fee. Where the applicant is (or all applicants are) so entitled, the amount to be entered at H is 25% of the handling fee.</i>)		129.00	H
3. Total of prescribed fees Add the amounts entered at P and H and enter total in the TOTAL box		1,659.00	
		TOTAL	
MODE OF PAYMENT			
☐ authorization to charge deposit account with the IPEA (see below)	☐ cash		
☐ cheque	☐ revenue stamps		
☐ postal money order	☐ coupons		
☐ bank draft	☒ other (specify): wire transfer		
AUTHORIZATION TO CHARGE (OR CREDIT) DEPOSIT ACCOUNT. (This mode of payment may not be available at all IPEAs)			
☐ Authorization to charge the total fees indicated above.		IPEA/	
☐ (This check-box may be marked only if the conditions for deposit accounts of the IPEA so permit) Authorization to charge any deficiency or credit any overpayment in the total fees indicated above.		Deposit Account No.:	
		Date:	
		Name:	
		Signature:	

McDermott Will & Emery

Boston Brussels Chicago Düsseldorf London Los Angeles Miami Milan
Munich New York Orange County Rome San Diego Silicon Valley Washington, D.C.

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1353
Cameron K. Wallerbach
Counsel
cwallerbach@mwe.com
202.756.8171

April 20, 2005

In re Application of: Yasumichi Fukuda
Application No.: PCT/US2004/020734
Filed: June 29, 2004
For: CYCLOPROPYL GROUP SUBSTITUTED OXAZOLIDINONE
ANTIBIOTICS AND DERIVATIVES THEREO

Attorney Docket No.: 50193-187

International Searching Authority: European Patent Office
PB 5818 Patentlaan 2
NL-2280 HV Rijswijk
Attn: ISA/EP Authorized Officer

RESPONSE TO WRITTEN OPINION

Sir or Madame:

This is in response to the Written Opinion dated 21 February 2005 in this application.

The Written Opinion noted that a copy of the earlier applications, whose priority has been claimed, has not been furnished. Our records show that the Receiving Office was requested to provide certified copies of two U.S. Provisional Application Nos. 60/483,904 and 60/546,984. A copy of the request is attached. Apparently, only one of the applications, namely, U.S. Provisional Application Nos. 60/483,904, was provided. See attached communication from the Receiving Office dated September 24, 2004. We have ordered a

certified copy of U.S. Provisional Application No. 60/546,984 (as attached) and will forward the same to the International Bureau of WIPO upon receipt.

The specification has been amended to correct obvious errors in the nomenclature of the formulae in Examples 15, 16, 22, 28, 34, 35, 44, 45, 90, 91 and 106-109. Please replace pages 40, 41, 45, 48, 52, 53, 59, 91 and 101-103. Specifically, the nomenclature for Example 15 on page 40 has been amended to indicate the correct position of the bicyclo[3.1.0] ring on the fluorophenyl ring as being at the 4 position. The nomenclature for Examples 16, 22, 28, 34, 35, 44, 45, 90, 91 and 106-109 on pages 41, 45, 48, 52, 53, 59, 91 and 101-103, respectively, has been amended to indicate the correct position of the bicyclo[3.1.0] ring on the pyridine ring as being at the 2 position. Entry of the replacement pages is requested.

The claims have been amended as follows. Claim 1 has been amended to delete "or a

C₅-10 heteroaryl represented by N which represents an optionally substituted aromatic heterocyclic group containing 1 to 4 nitrogen atoms and at least one double bond, and which is connected through a bond on any nitrogen said heteroaryl optionally substituted with 1 to 3

substituents selected from R₇." In addition, Ar or HAr Ar or HAr had been limited to represent aryl or heteroaryl only. Claims 7 and 8 have been deleted. Claim 10 has been amended to delete the following two compounds: 1-[5(R)-3-[3-Fluoro-4-[2-(1-methyltetrazol-5-yl)pyridin-5-yl]phenyl]-2-oxooxa-zolidin-5-ylmethyl]-1,2,3-triazole and 1-[5(R)-3-[3,5-Difluoro-4-[2-(1-methyltetrazol-5-yl)pyridin-5-yl]phenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole. Claim 11 has been amended to delete the following compound: 1-[5(R)-3-[3-Fluoro-4-[2-(1-methyltetrazol-5-yl)pyridin-5-yl]phenyl]-2-oxooxa-zolidin-5-ylmethyl]-1,2,3-

Application No.: PCT/US2004/020734

triazole. All of the claims, including the amended claims, claims are submitted herewith on substitute pages 150-174 which are attached to this response. Entry of the substitute claims is respectfully requested.

Applicant notes that the Written Opinion indicated that although claims 14 and 15 are covered by the provisions of Rule 67.1(v) PCT, that no opinion has been rendered as to the industrial applicability of the subject matter of the claims.

The Written Opinion stated that substituent Y as it relates to "CN" was unclear because Y is divalent. The "CN" moiety has been deleted from the "Y" grouping in claim 1.

The Written Opinion stated that with respect to defining X in claim 1 as being a heterocycle N, the expression "aromatic heterocyclic group containing 1-4 nitrogen atoms and at least one double bond" was confusing. The expression has been deleted from claim 1.

The Written Opinion indicates that there is no unity of invention. Claim 1 has been amended to delete the N-bound saturated ring and also that Ar is aryl and HAr is a heterocyclic aromatic. Also, claims 7 and 8 directed to the N-bound saturated ring of the oxazolidinone ring have been canceled. Accordingly, reconsideration of the holding of lack of unity of the invention is requested since the invention is directed to X being the bicyclo[3.1.0]-ring system..

In view of the amendments to the claims, the Written Opinion with respect to "invention 2" is now moot. As for "invention 1", it would appear from the Written Opinion that claims directed to X being the bicyclo[3.1.0] ring system would satisfy the novelty and inventive steps.

Application No.: PCT/US2004/020734

For all of the foregoing reasons, reconsideration of the application is requested.

Respectfully submitted,

McDERMOTT WILL & EMERY LLP



Cameron K. Weiffenbach

600 13th Street, N.W.
Washington, DC 20005-3096
Phone: 202.756.8000 CKW:ckw
Facsimile: 202.756.8087

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Box No. V DESIGNATIONS

The filing of this request constitutes under Rule 4.9(a), the designation of all Contracting States bound by the PCT on the international filing date, for the grant of every kind of protection available and, where applicable, for the grant of both regional and national patents.

However,

- ☐ DE Germany is not designated for any kind of national protection
- ☐ KR Republic of Korea is not designated for any kind of national protection
- ☐ RU Russian Federation is not designated for any kind of national protection

(The check-boxes above may be used to exclude (irrevocably) the designations concerned in order to avoid the ceasing of the effect, under the national law, of an earlier national application from which priority is claimed. See the Notes to Box No. V as to the consequences of such national law provisions in these and certain other States.)

Box No. VI PRIORITY CLAIM

The priority of the following earlier application(s) is hereby claimed:

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country or Member	regional application: regional Office	international application: receiving Office
item (1) 02 July 2003 (02.07.03)	60/483,904	US		
item (2) 24 February 2004 (24.02.04)	60/546,984	US		
item (3)				

- ☐ Further priority claims are indicated in the Supplemental Box.

The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of this international application is the receiving Office) identified above as:

- ☒ all items ☐ item (1) ☐ item (2) ☐ item (3) ☐ other, see Supplemental Box

* Where the earlier application is an ARIPO application, indicate at least one country party to the Paris Convention for the Protection of Industrial Property or one Member of the World Trade Organization for which that earlier application was filed (Rule 4.10(b)(ii)):

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) (if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):

ISA/ EPO

Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):

Date (day/month/year)

Number

Country (or regional Office)

Box No. VIII DECLARATIONS

The following declarations are contained in Boxes Nos. VIII (i) to (v) (mark the applicable check-boxes below and indicate in the right column the number of each type of declaration):

Number of declarations

- ☐ Box No. VIII (i) Declaration as to the identity of the inventor
- ☐ Box No. VIII (ii) Declaration as to the applicant's entitlement, as at the international filing date, to apply for and be granted a patent
- ☐ Box No. VIII (iii) Declaration as to the applicant's entitlement, as at the international filing date, to claim the priority of the earlier application
- ☐ Box No. VIII (iv) Declaration of inventorship (only for the purposes of the designation of the United States of America)
- ☐ Box No. VIII (v) Declaration as to non-prejudicial disclosures or exceptions to lack of novelty:

RECEIVED
14 OCT 2004

PATENT COOPERATION TREATY

PCT/US04/020734

From the INTERNATIONAL BUREAU

PCT

**NOTIFICATION CONCERNING
SUBMISSION OR TRANSMITTAL
OF PRIORITY DOCUMENT**

(PCT Administrative Instructions, Section 411)

To:

1063

TOFFENETTI, Judith, L.
McDermott, Will & Emery LLP
600 13th Street, N.W.
Washington, DC 20005-3088
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 29 September 2004 (29.09.2004)	
Applicant's or agent's file reference 60183-167	IMPORTANT NOTIFICATION
International application No. PCT/US04/020734	International filing date (day/month/year) 29 June 2004 (29.06.2004)
International publication date (day/month/year)	Priority date (day/month/year) 02 July 2003 (02.07.2003)
Applicant MERCK & CO., INC. et al	

- By means of this Form, which replaces any previously issued notification concerning submission or transmittal of priority documents, the applicant is hereby notified of the date of receipt by the International Bureau of the priority document(s) relating to all earlier application(s) whose priority is claimed. Unless otherwise indicated by the letters "NR" in the right-hand column or by an asterisk appearing next to a date of receipt, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- (If applicable) The letters "NR" appearing in the right-hand column denote a priority document which, on the date of receipt of this Form, had not yet been received by the International Bureau under Rule 17.1(a) or (b). Where, under Rule 17.1(a), the priority document must be submitted by the applicant to the receiving Office or the International Bureau, but the applicant fails to submit the priority document within the applicable time limit under that Rule, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- (If applicable) An asterisk (*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b) (the priority document was received after the time limit prescribed in Rule 17.1(a) or the request to prepare and transmit the priority document was submitted to the receiving Office after the applicable time limit under Rule 17.1(b)). Even though the priority document was not furnished in compliance with Rule 17.1(a) or (b), the International Bureau will nevertheless transmit a copy of the document to the designated Offices, for their consideration. In case such a copy is not accepted by the designated Office as the priority document, Rule 17.1(c) provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
02 July 2003 (02.07.2003)	60483,904	US	30 August 2004 (30.08.2004)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

Cruz Juan

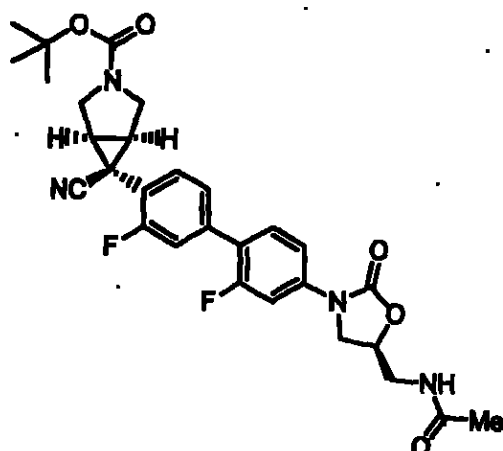
Facsimile No. +41 22 740 14 35

Facsimile No. +41 22 338 89 65

Telephone No. +41 22 338 8239

Form PCT/IB/304 (January 2004)

EXAMPLE 14



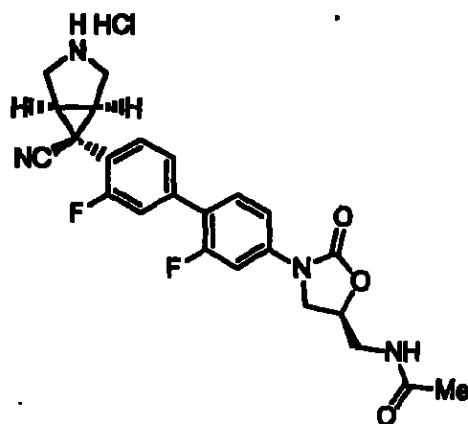
N-[5(S)-3-[4-[4-[(1 α ,5 α ,6 β)-3-t-Butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3-fluorophenyl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide.

The title compound 14 (24.9 mg) was prepared from N-[5(S)-3-[3-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaboroly)phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide (20.0 mg) and 1-bromo-4-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3-fluorobenzene (20.2 mg) in the same manner as described for EXAMPLE 1.

MS (FAB⁺) *m/z*: 553 (MH⁺).

HRMS (FAB⁺) for C₂₈H₃₁F₃N₄O₅ (MH⁺): calcd, 553.2263; found, 553.2250.

EXAMPLE 15



N-[5(S)-3-[4-[4-[(1 α ,5 α ,6 β)-6-Cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3-fluorophenyl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide Hydrochloride.

SUBSTITUTE

208

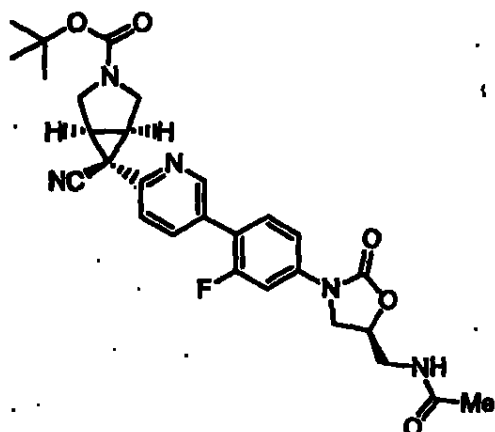
The title compound 15 (290 mg) was prepared from N-[5(S)-3-[4-[4-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3-fluorophenyl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide (367 mg)

in the same manner as described for EXAMPLE 2.

MS (FAB⁺) *m/z*: 453 (MH⁺) (as free base).

HRMS (FAB⁺) for C₂₄H₂₃F₂N₄O₅ (MH⁺): calcd, 453.1738; found, 453.1747.

EXAMPLE 16



N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide.

The title compound 16 (354 mg) was prepared from N-[5(S)-3-[3-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolyl)phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide (350 mg) and 5-bromo-2-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridine (337 mg) in the same manner as described for EXAMPLE 1.

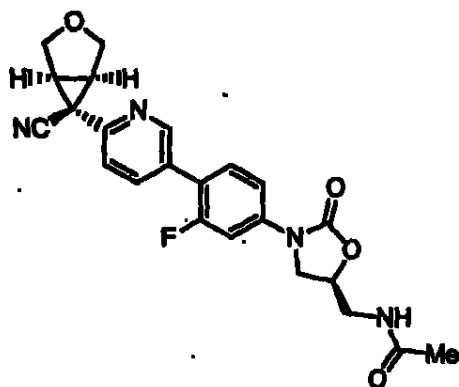
MS (FAB⁺) *m/z*: 536 (MH⁺).

HRMS (FAB⁺) for C₂₈H₃₁FN₅O₅ (MH⁺): calcd, 536.2309; found, 536.2296.

SUBSTITUTE

HRMS (FAB⁺) for C₂₂H₂₂FN₆O₃ (MH⁺): calcd, 437.1737; found, 437.1755.

EXAMPLE 22



N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-Cyano-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide.

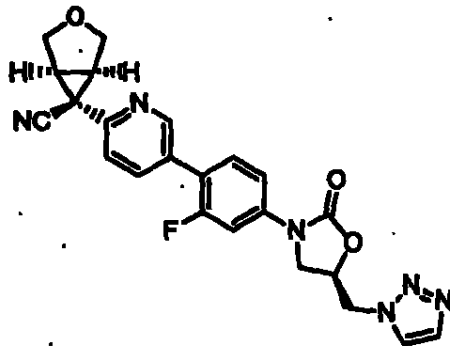
The title compound 22 (302 mg) was prepared from N-[5(S)-3-[3-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolyl)phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide (378 mg) and 5-bromo-2-[(1 α ,5 α ,6 β)-6-cyano-3-oxabicyclo[3.1.0]hexan-6-yl]pyridine (337 mg) in the same manner as described for

EXAMPLE 1.

MS (EI⁺) *m/z*: 436 (M⁺).

HRMS (EI⁺) for C₂₂H₂₁FN₆O₄ (M⁺): calcd, 436.1547; found, 436.1516.

EXAMPLE 23



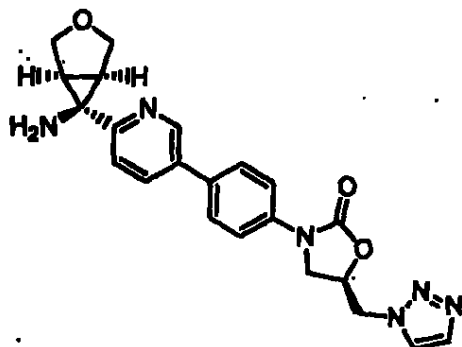
1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-Cyano-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole.

SUBSTITUTE

MS (FAB⁺) *m/z*: 519 (MH⁺).

HRMS (FAB⁺) for C₂₇H₃₁N₆O₅ (MH⁺): calcd, 519.2356; found, 519.2382.

EXAMPLE 27



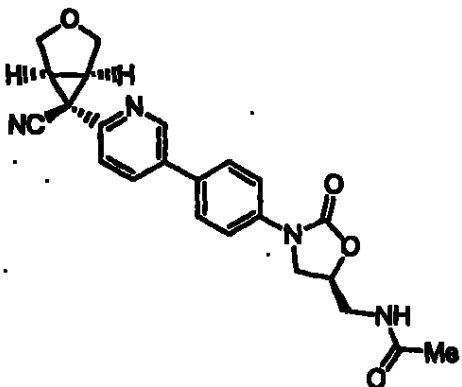
1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-Amino-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]phenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole.

The title compound 27 (210 mg) was prepared from 1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-*t*-butoxycarbonylamino-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]phenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole (310 mg) in the same manner as described for EXAMPLE 18.

MS (FAB⁺) *m/z*: 419 (MH⁺).

HRMS (FAB⁺) for C₂₂H₂₃N₆O₅ (MH⁺): calcd, 419.1832; found, 419.1835.

EXAMPLE 28

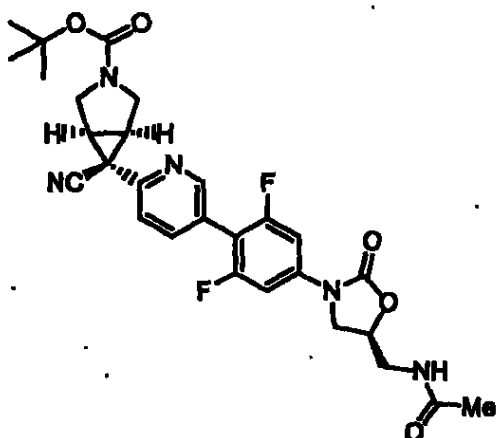


N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-Cyano-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide.

SUBSTITUTE

Title Compound 33 (281 mg) was prepared from 1-[5(R)-3-[4-[4-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3,5-difluorophenyl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole (360 mg) in the same manner as described for EXAMPLE 2.
 MS (FAB⁺) m/z: 481 (MH⁺) (as free base).
 HRMS (FAB⁺) for C₂₄H₂₈F₃N₄O₂ (MH⁺): calcd, 481.1600; found, 481.1598.

EXAMPLE 34



N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-3-t-Butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide.

Title Compound 34 (15.5 mg) was prepared from N-[5(S)-3-[3,5-difluoro-4-(trifluoromethanesulfonyl)oxyphenyl]-2-oxooxazolidin-5-ylmethyl]acetamide (19.6 mg) and 5-bromo-2-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridine (20.0 mg) in the same manner as described for

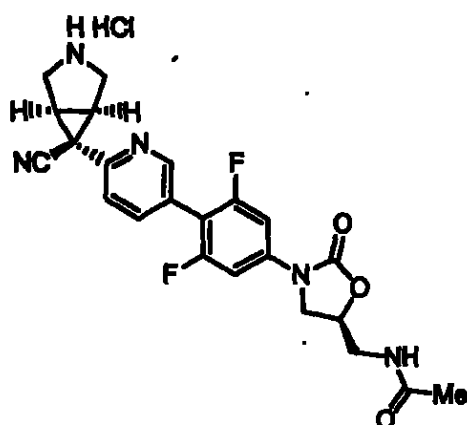
EXAMPLE 31.

MS (FAB⁺) m/z: 554 (MH⁺).

HRMS (FAB⁺) for C₂₈H₃₀F₂N₅O₅ (MH⁺): calcd, 554.2215; found, 554.2201.

EXAMPLE 35

SUBSTITUTE



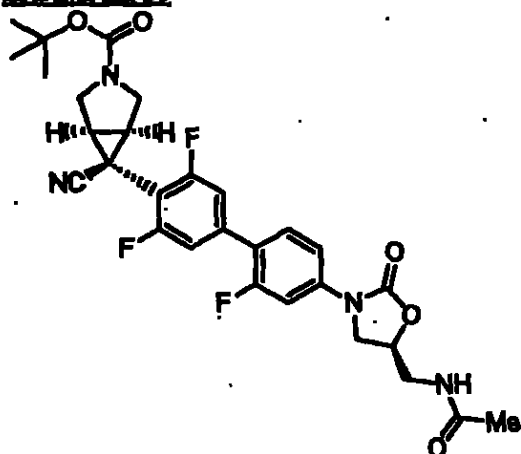
N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-Cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide Hydrochloride.

Title Compound 35 (185 mg) was prepared from N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-3-*t*-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide (235 mg) in the same manner as described for EXAMPLE 2.

MS (FAB⁺) *m/z*: 454 (MH⁺) (as free base).

HRMS (FAB⁺) for C₂₃H₂₂F₂N₅O₃ (MH⁺): calcd, 454.1691.; 454.1651.

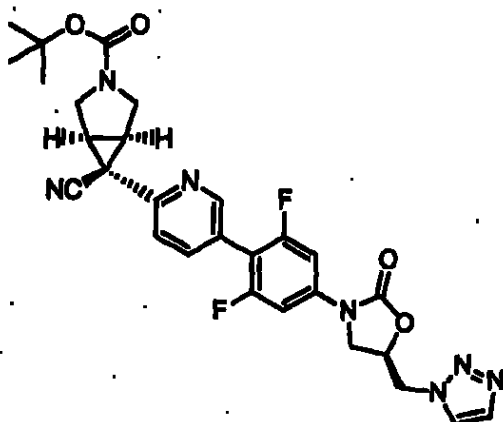
EXAMPLE 36



N-[5(S)-3-[4-[4-[(1 α ,5 α ,6 β)-3-*t*-Butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3,5-difluorophenyl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide.

Title Compound 36 (347 mg) was prepared from N-[5(S)-3-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolyl)-3-fluorophenyl]-

SUBSTITUTE



1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-3-t-Butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole.

Title Compound 44 (14.5 mg) was prepared from 1-[5(R)-3-[3,5-difluoro-4-(trifluoromethanesulfonyloxyphenyl]-

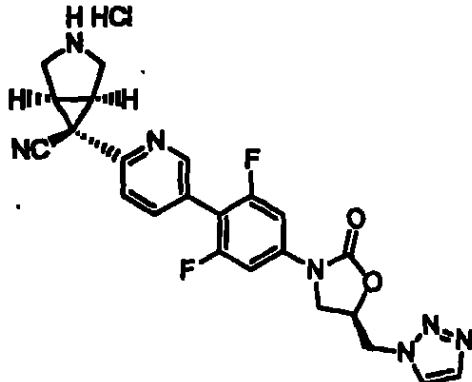
2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole (19.6 mg) and 5-bromo-2-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-

cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridine (20.0 mg) in the same manner as described for EXAMPLE 31.

MS (FAB⁺) *m/z*: 564 (MH⁺).

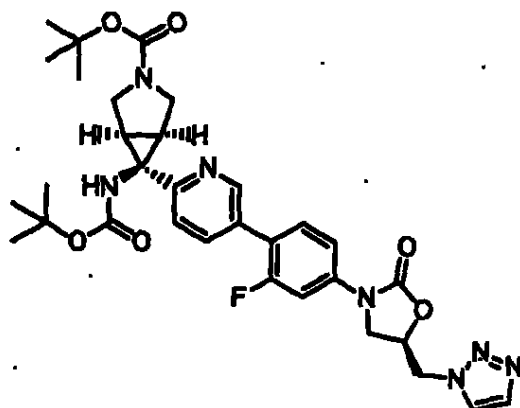
HRMS (FAB⁺) for C₂₈H₂₈F₂N₇O₄ (MH⁺): calcd, 564.2171; found, 564.2147.

EXAMPLE 45



1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-Cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole Hydrochloride.

SUBSTITUTE



1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-3-t-Butoxycarbonyl-6-(t-butoxycarbonyl)amino-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole.

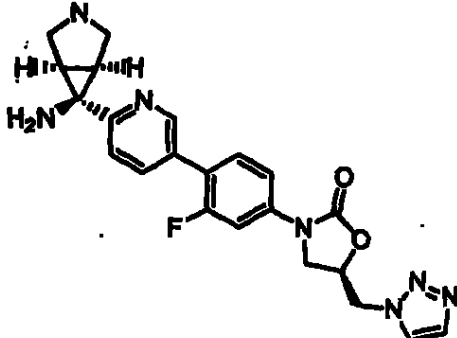
Title Compound 90 (473 mg) was prepared from 1-[5(R)-3-[3-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolyl)-phenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole (600 mg) and 5-bromo-2-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-(t-butoxycarbonyl)amino-3-azabicyclo[3.1.0]hexan-6-yl]pyridine (702 mg) in the same manner as described for EXAMPLE 1.

MS (FAB⁺) *m/z*: 636 (MH⁺).

HRMS (FAB⁺) for C₂₂H₂₈N₇O₆ (MH⁺): calcd, 636.2946; found, 636.2931.

EXAMPLE 91

H 2HCl



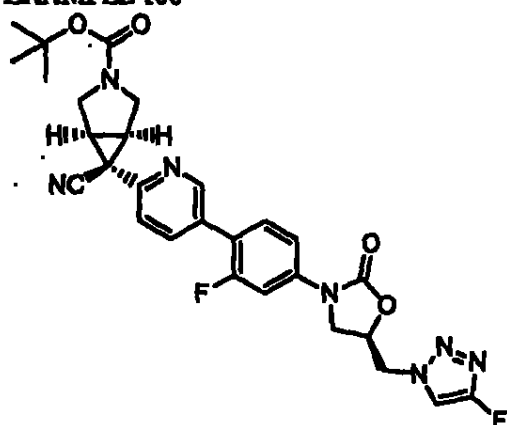
1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-Amino-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole Dihydrochloride.

Title Compound 91 (305 mg) was prepared from 1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-(t-butoxycarbonyl)-amino-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-

SUBSTITUTE

HRMS (FAB⁺) for C₂₃H₁₉F₂N₄O₃ (MH⁺): calcd, 465.1487; found, 465.1514.

EXAMPLE 106



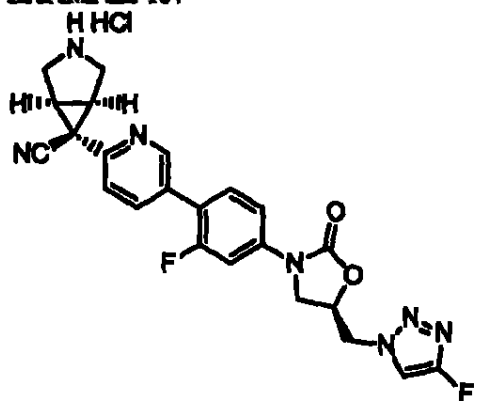
1-[5(R)-3-[4-{2-[(1 α ,5 α ,6 β)-3-t-Butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-4-fluoro-1,2,3-triazole.

Title Compound 106 (301 mg) was prepared from 4-fluoro-1-[5(R)-3-[3-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolyl)phenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole (370 mg) and 5-bromo-2-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridine (332 mg) in the same manner as described for EXAMPLE 1.

MS (FAB⁺) *m/z*: 564 (MH⁺).

HRMS (FAB⁺) for C₂₈H₂₈F₂N₇O₄ (MH⁺): calcd, 564.2171; found, 564.2168.

EXAMPLE 107



SUBSTITUTE

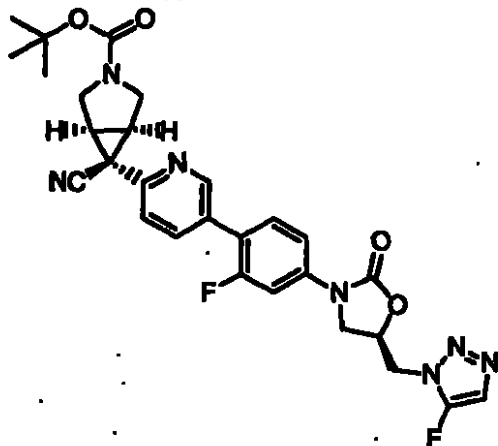
1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-Cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-4-fluoro-1,2,3-triazole Hydrochloride.

Title Compound 107 (231 mg) was prepared from 1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-4-fluoro-1,2,3-triazole (290 mg) in the same manner as described for EXAMPLE 2.

MS (FAB⁺) *m/z*: 464 (MH⁺) (as free base).

HRMS (FAB⁺) for C₂₃H₂₂F₂N₇O₂ (MH⁺): calcd, 464.1647; found, 464.1645.

EXAMPLE 108



1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-3-t-Butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-5-fluoro-1,2,3-triazole.

Title Compound 108 (169 mg) was prepared from 1-[5(R)-3-(3-fluoro-4-iodophenyl)-2-oxooxazolidin-5-ylmethyl]-5-fluoro-1,2,3-triazole (150 mg) and 5-bromo-2-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo-[3.1.0]hexan-6-yl]pyridine (202 mg) in the same manner as described for EXAMPLE 31.

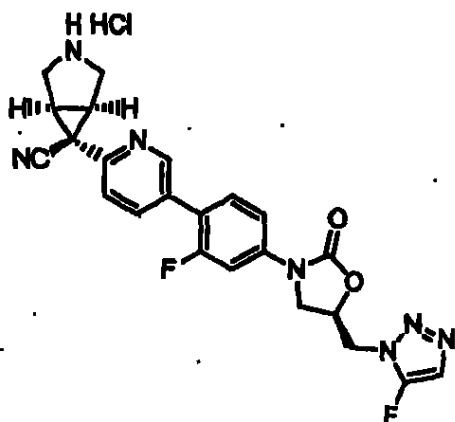
MS (FAB⁺) *m/z*: 564 (MH⁺).

HRMS (FAB⁺) for C₂₈H₂₈F₂N₇O₄ (MH⁺): calcd, 564.2171; found, 564.2189.

EXAMPLE 109

SUBSTITUTE

217



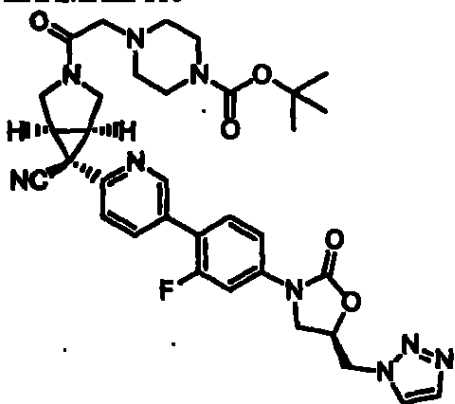
1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-Cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-5-fluoro-1,2,3-triazole Hydrochloride.

Title Compound 109 (118 mg) was prepared from 1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-3-*t*-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-5-fluoro-1,2,3-triazole (151 mg) in the same manner as described for EXAMPLE 2.

MS (FAB⁺) *m/z*: 464 (MH⁺) (as free base).

HRMS (FAB⁺) for C₂₂H₂₃F₂N₇O₂ (MH⁺): calcd, 464.1647; found, 464.1679.

EXAMPLE 110



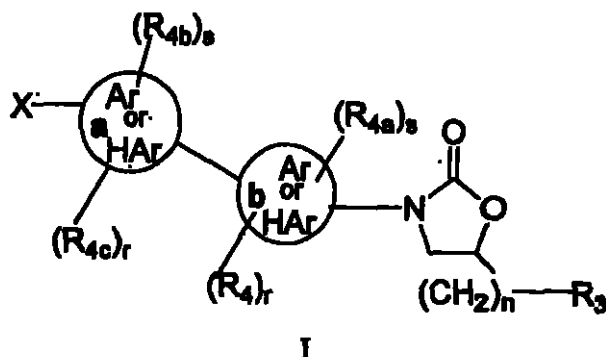
1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-3-(4-*t*-Butoxycarbonylpiperazin-1-yl)acetyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole.

Title compound 110 (60.7 mg) was prepared from 1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-

SUBSTITUTE

What is Claimed Is:

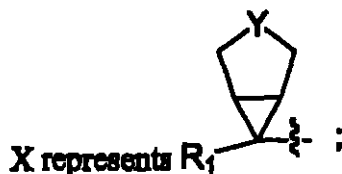
1. The present invention relates to compounds of formula I:



its enantiomer, diastereomer, or pharmaceutically acceptable salt, hydrate or prodrug thereof wherein:

R₁ represents

- i) hydrogen,
- ii) (CH₂)_nNR₅R₆,
- iii) CR₇R₈R₉, C(R)₂OR₁₄, CH₂NHR₁₄,
- iv) C(=O)R₁₃, C(=NOH)H, C(=NOR₁₃)H, C(=NOR₁₃)R₁₃, C(=NOH)R₁₃, C(=O)N(R₁₃)₂, C(=NOH)N(R₁₃)₂, NHC(=X₁)N(R₁₃)₂, NRCO₂R, (C=NH)R₇, N(R₁₃)C(=X₁)N(R₁₃)₂, COOR₁₃, SO₂R₁₄, N(R₁₃)SO₂R₁₄, N(R₁₃)COR₁₄,
- v) (C₁₋₆alkyl)CN, CN, CH=C(R)₂, (CH₂)_pOH, C(=O)CHR₁₃, C(=NR₁₃)R₁₃, NR₁₀C(=X₁)R₁₃; or
- vi) C₅-10 heterocycle optionally substituted with 1-3 groups of R₇, which may be attached through either a carbon or a heteroatom;



Y represents NR^* , O or $\text{S}(\text{O})_p$;



represents aryl or heteroaryl;

R_3 represents $\text{NR}(\text{C}=\text{X}_2)\text{R}_{12}$, NR^*R_{12} , $\text{C}_6\text{-10}$ aryl, or $-(\text{O})_n\text{C}_5\text{-10}$ heterocyclyl which may be attached through either a carbon or a heteroatom; said aryl and heterocyclyl optionally substituted with 1-3 groups of R_7 ,

R_4 , R_{4a} , R_{4b} , and R_{4c} independently represent

- i) hydrogen,
- ii) halogen,
- iii) $\text{C}_1\text{-6}$ alkoxy, or
- iv) $\text{C}_1\text{-6}$ alkyl;

r and s independently are 1-3, with the provision that when $(\text{R}_{4a})_r$ and $(\text{R}_4)_r$ or $(\text{R}_{4b})_s$ and $(\text{R}_{4c})_s$ are attached to an Ar or HAr ring the sum of r and s is less than or equal to 4;

R_5 and R_6 independently represent

- i) hydrogen,
- ii) $\text{C}_1\text{-6}$ alkyl optionally substituted with 1-3 groups of halogen, CN, OH, $\text{C}_1\text{-6}$ alkoxy, amino, imino, hydroxyamino, alkoxyamino, $\text{C}_1\text{-6}$ acyloxy, $\text{C}_1\text{-6}$ alkylsulfenyl, $\text{C}_1\text{-6}$ alkylsulfinyl, $\text{C}_1\text{-6}$ alkylsulfonyl, aminosulfonyl, $\text{C}_1\text{-6}$ alkylaminosulfonyl, $\text{C}_1\text{-6}$ dialkylaminosulfonyl, 4-morpholinylsulfonyl, phenyl, pyridine, 5-isoxazolyl, ethylenyloxy, or ethynyl, said phenyl and pyridine optionally substituted with 1-3 halogen, CN, OH, CF_3 , $\text{C}_1\text{-6}$ alkyl or $\text{C}_1\text{-6}$ alkoxy;

SUBSTITUTE

iii) C₁₋₆ acyl optionally substituted with 1-3 groups of halogen, OH, SH, C₁₋₆ alkoxy, naphthalenoxy, phenoxy, amino, C₁₋₆ acylamino, hydroxylamino, alkoxylamino, C₁₋₆ acyloxy, aralkyloxy, phenyl, pyridine, C₁₋₆ alkylcarbonyl, C₁₋₆ alkylamino, C₁₋₆ dialkylamino, C₁₋₆ hydroxyacyloxy, C₁₋₆ alkylsulfonyl, phthalimido, maleimido, succinimido, said phenoxy, phenyl and pyridine optionally substituted with 1-3 groups of halo, OH, CN, C₁₋₆ alkoxy, amino, C₁₋₆ acylamino, CF₃ or C₁₋₆ alkyl;

iv) C₁₋₆ alkylsulfonyl optionally substituted with 1-3 groups of halogen, OH, C₁₋₆ alkoxy, amino, hydroxylamino, alkoxylamino, C₁₋₆ acyloxy, or phenyl; said phenyl optionally substituted with 1-3 groups of halo, OH, C₁₋₆ alkoxy, amino, C₁₋₆ acylamino, CF₃ or C₁₋₆ alkyl;

v) arylsulfonyl optionally substituted with 1-3 of halogen, C₁₋₆ alkoxy, OH or C₁₋₆ alkyl;

vi) C₁₋₆ alkoxycarbonyl optionally substituted with 1-3 of halogen, OH, C₁₋₆ alkoxy, C₁₋₆ acyloxy, or phenyl, said phenyl optionally substituted with 1-3 groups of halo, OH, C₁₋₆ alkoxy, amino, C₁₋₆ acylamino, CF₃ or C₁₋₆ alkyl;

vii) aminocarbonyl, C₁₋₆ alkylaminocarbonyl or C₁₋₆ dialkylaminocarbonyl, said alkyl groups optionally substituted with 1-3 groups of halogen, OH, C₁₋₆ alkoxy or phenyl

viii) five to six membered heterocycles optionally substituted with 1-3 groups of halogen, OH, CN, amino, C₁₋₆ acylamino, C₁₋₆ alkylsulfonylamino, C₁₋₆ alkoxycarbonylamino, C₁₋₆ alkoxy, C₁₋₆ acyloxy or C₁₋₆ alkyl, said alkyl optionally substituted with 1-3 groups of halogen, or C₁₋₆ alkoxy;

ix) C₃₋₆ cycloalkylcarbonyl optionally substituted with 1-3 groups of halogen, OH, C₁₋₆ alkoxy or CN;

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- x) benzoyl optionally substituted with 1-3 groups of halogen, OH, C1-6 alkoxy, C1-6 alkyl, CF₃, C1-6 alkanoyl, amino or C1-6 acylamino;
- xi) pyrrolylcarbonyl optionally substituted with 1-3 of C1-6 alkyl;
- xii) C1-2 acyloxyacetyl where the acyl is optionally substituted with amino, C1-6 alkylamino, C1-6 dialkylamino, 4-morpholino, 4-aminophenyl, 4-(dialkylamino)phenyl, 4-(glycylamino)phenyl; or

R₅ and R₆ taken together with any intervening atoms can form a 3 to 7 membered heterocyclic ring containing carbon atoms and 1-2 heteroatoms independently chosen from O, S, SO, SO₂, N, or NR₃;

R₇ represents

- i) hydrogen, halogen, (CH₂)_pC₃₋₁₀ heterocyclyl, CN, CO₂R, CON(R)₂, CHO, (CH₂)₀₋₃NHAc, C(=NOR), OH, C1-6 alkoxy, C1-6 alkyl, alkenyl, hydroxy C1-6 alkyl, (CH₂)₁₋₃NHC(O)C1-6 alkyl, (CH₂)₀₋₃N(C1-6 alkyl)₂, NHCO₂R, -OCOC1-6 alkyl;
- ii) (CH₂)_namino, (CH₂)_nC1-6 alkylamino, C1-6 acylamino, C1-6 dialkylamino, hydroxylamino or C1-2 alkoxyamino all of which can be optionally substituted on the nitrogen with C1-6 acyl, C1-6 alkylsulfonyl or C1-6 alkoxycarbonyl, said acyl and alkylsulfonyl optionally substituted with 1-2 of halogen or OH;

R₈ and R₉ independently represent

- i) H, CN,
- ii) C1-6 alkyl optionally substituted with 1-3 halogen, CN, OH, C1-6 alkoxy, C1-6 acyloxy, or amino,

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iii) phenyl optionally substituted with 1-3 groups of halogen, OH, C₁₋₆ alkoxy; or

R₇ and R₈ taken together can form a 3-7 membered carbon ring optionally interrupted with 1-2 heteroatoms chosen from O, S, SO, SO₂, NH, and NR₈;

X₁ represents O, S or NR₁₃, NCN, NCO₂R₁₆, or NSO₂R₁₄

X₂ represents O, S, NH or NSO₂R₁₄;

R₁₀ represents hydrogen, C₁₋₆ alkyl or CO₂R₁₅;

R₁₂ represents hydrogen, C₁₋₆ alkyl, NH₂, OR, CHF₂, CHCl₂, C(R)₂Cl, (CH₂)_nSR, (CH₂)_nCN, (CH₂)_nSO₂R, (CH₂)_nS(O)R, C₁₋₆ alkylamino, C₃₋₆ cycloalkyl, C₅₋₁₀ heterocyclyl or C₁₋₆ dialkylamino, where said alkyl, and cycloalkyl may be substituted with 1-3 groups of halo, CN, OH or C₁₋₆ alkoxy, said heterocyclyl optionally substituted with 1-3 groups of R₇;

each R₁₃ represents independently hydrogen, C₁₋₆ alkyl, C₆₋₁₀ aryl, NR₅R₆, SR₈, S(O)R₈, S(O)₂R₈, CN, OH, C₁₋₆ alkylS(O)R, C₁₋₆ alkoxy carbonyl, hydroxycarbonyl, -OCOaryl, C₁₋₆ acyl, C₃₋₇ membered carbon ring optionally interrupted with 1-4 heteroatoms chosen from O, S, SO, SO₂, NH and NR₈ where said C₁₋₆ alkyl, aryl or C₁₋₆ acyl groups may be independently substituted with 0-3 halogens, hydroxy, N(R)₂, CO₂R, C₆₋₁₀ aryl, C₅₋₁₀ heteroaryl, or C₁₋₆ alkoxy groups;

when two R₁₃ groups are attached to the same atom or two adjacent atoms they may be taken together to form a 3-7 membered carbon ring optionally interrupted with 1-2 heteroatoms chosen from O, S, SO, SO₂, NH, and NR₈;

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R represents hydrogen or C₁₋₆ alkyl;

R* represents hydrogen, CN, C(=O)R₁₄, (CH₂)_pCO₂C₁₋₆ alkyl, (CH₂)_pC₅₋₁₀heterocyclyl, or C₁₋₆ alkyl, said alkyl and heterocyclyl optionally substituted with 1 to 3 groups of R₇;

R₁₄ represents amino, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, (CH₂)_pC₅₋₁₀heterocyclyl, C₁₋₆ haloalkyl, phenyl, said alkyl, cycloalkyl, phenyl, heterocyclyl optionally substituted with 1-3 group of R₇, when R₇ is an amino or hydroxyl group or a nitrogen that forms part of the heterocycle, said amino and hydroxy optionally protected with an amino or hydroxy protecting group;

R₁₅ is C₁₋₆ alkyl or benzyl said benzyl optionally substituted with 1-3 groups of halo, OH, C₁₋₆ alkoxy, amino, C₁₋₆ acylamino, or C₁₋₆ alkyl;

R₁₆ is hydrogen, C₅₋₁₀heteroaryl, C₆₋₁₀aryl, said heteroaryl and aryl optionally substituted with 1-3 groups of R₇;

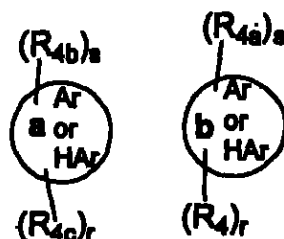
p represents 0-2 and

n represents 0.

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2. The compound according to claim 1 wherein Ar and HAr of



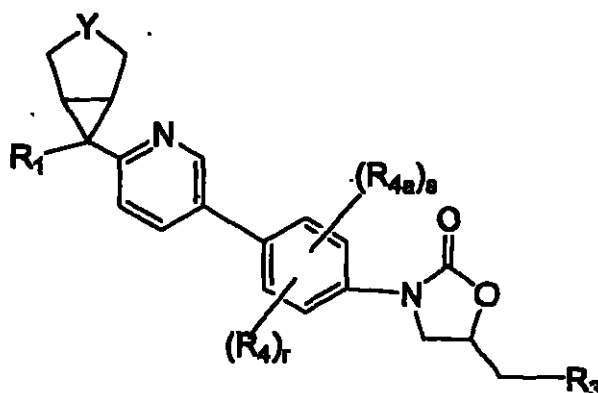
independently are phenyl, pyridyl, pyrimidinyl, or piperidinyl, and $r + s$ for a and b combined ≤ 3 .



3. The compound according to claim 2 wherein X is R_1
4. The compound according to claim 3 wherein Y is NR^* and R_1 is H, NR_5R_6 , CN, OH, or $CR_7R_8R_9$.
5. The compound according to claim 4 wherein R_1 is NR_5R_6 , or CN.
6. The compound according to claim 5 wherein R_3 is C5-10 heteroaryl, said heteroaryl optionally substituted with 1-3 groups of R_7

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9. The compound according to claim 1 of the structural formula IV:



Formula IV

wherein R_4 , R_{4a} , are as described and R_3 and $\textcircled{N}$ independently are 1,2,3-triazole, 1,2,4-triazole, 1,2,5-triazole, tetrazole, pyrazole, or imidazole, any of which may contain 1 to 3 substituents selected from R_7 .

10. A compound which is;

1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]phenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]phenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole hydrochloride,

1-[5(R)-3-[4-[4-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3-fluorophenyl]phenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

1-[5(R)-3-[4-[4-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3-fluorophenyl]phenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole hydrochloride,

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1-[5(R)-3-[4-[4-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3-fluorophenyl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

1-[5(R)-3-[4-[4-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3-fluorophenyl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole hydrochloride,

1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole hydrochloride,

N-[5(S)-3-[4-[4-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3-fluorophenyl]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

N-[5(S)-3-[4-[4-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3-fluorophenyl]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide hydrochloride,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide hydrochloride,

N-[5(S)-3-[4-[4-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3-fluorophenyl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3-fluorophenyl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide hydrochloride,

N-[5(S)-3-[4-[4-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide hydrochloride,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-t-butoxycarbonylamino-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-amino-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

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1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-t-butoxycarbonylamino-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-amino-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

N-[5(S)-3-[4-[4-[(1 α ,5 α ,6 β)-6-cyano-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-t-butoxycarbonylamino-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-amino-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-t-butoxycarbonylamino-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]phenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-amino-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]phenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

N-[5(S)-3-[4-[4-[(1 α ,5 α ,6 β)-6-cyano-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]phenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

1-[5(R)-3-[4-[4-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3,5-difluorophenyl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

1-[5(R)-3-[4-[4-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3,5-difluorophenyl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

N-[5(S)-3-[4-[4-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

N-[5(S)-3-[4-[4-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide hydrochloride,

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N-[5(S)-3-[4-[4-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3,5-difluorophenyl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

N-[5(S)-3-[4-[4-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3,5-difluorophenyl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide hydrochloride,

N-[5(S)-3-[4-[4-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]phenyl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

N-[5(S)-3-[4-[4-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]phenyl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

N-[5(S)-3-[4-[4-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3-fluorophenyl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

N-[5(S)-3-[4-[4-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3-fluorophenyl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

1-[5(R)-3-[4-[4-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3-fluorophenyl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

1-[5(R)-3-[4-[4-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]-3-fluorophenyl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole hydrochloride,

1-[5(R)-3-[4-[4-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

1-[5(R)-3-[4-[4-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole

1-[5(R)-3-[4-[4-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]phenyl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

1-[5(R)-3-[4-[4-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]phenyl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-t-butoxycarbonylamino-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-amino-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

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N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-t-butoxycarbonylamino-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-amino-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3,5-difluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-thiabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-thiabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide S-oxide,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-thiabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]acetamide S,S-dioxide,

1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-thiabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,

1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-thiabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole S-oxide,

1-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-thiabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole S,S-dioxide,

4-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,4-triazole,

4-[5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,4-triazole,

5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-5-[(isoxazol-3-yl)oxy]methyloxazolidin-2-one,

5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-5-[(isoxazol-3-yl)oxy]methyloxazolidin-2-one,

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5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-5-[N-(t-butoxycarbonyl)-N-(isoxazol-3-yl)]aminomethyloxazolidin-2-one,

5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-5-[N-(isoxazol-3-yl)]aminomethyloxazolidin-2-one,

5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-5-[(isoxazol-3-yl)oxy]methyloxazolidin-2-one,

5(R)-5-[N-(t-butoxycarbonyl)-N-(isoxazol-3-yl)]aminomethyl-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]oxazolidin-2-one,

5(R)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-5-[N-(isoxazol-3-yl)]aminomethyloxazolidin-2-one,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]propionamide,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]difluoroacetamide,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-oxabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]cyclopropanecarboxamide,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]propionamide,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]propionamide,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]cyclopropanecarboxamide,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]cyclopropanecarboxamide,

N-[5(S)-3-[4-[2-[(1 α ,5 α ,6 β)-3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]pyridin-5-yl]-3-fluorophenyl]-2-oxooxazolidin-5-ylmethyl]difluoroacetamide,

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